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ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY

(Succeeding Vol. 38, 1919, the Journal of Cutaneous Diseases)

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VOLUME 4
1921

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PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

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Archives of Dermatology and Syphilology

VOLUME 4

JULY, 1921

NUMBER 1

RINGWORM OF THE NAILS

A PRELIMINARY REPORT OF SIXTEEN CASES OF ONYCHOMYCOSIS
WITH A CULTURAL STUDY OF TWELVE OF THESE
CASES DUE TO TRICHOPHYTONS

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This contribution is offered, largely, as a result of being a victim of ringworm of the nails for about thirty-five years. A final demonstration of its true nature and successful treatment has stimulated an interest in the fungi responsible for ringworm in this country, particularly the varieties that attack the nails.

Of perhaps greatest interest to the dermatologist have been some of the more obscure types of the disease, particularly of the hands and feet, conditions in many cases previously attributed to other causes. Owing to the rarity of the nail affection and greater difficulty of growing cultures from nail parings, comparatively little is known as to the species of fungi responsible for onychomycosis. This is particularly true in this country where systematic study of these fungi has been very much neglected.

The frequency of the nail affection, especially in the south, warrants, it is believed, a preliminary report of some work accomplished during the past three years. As fresh material may be secured from several of these cases, they afford a somewhat unusual opportunity for further cultural study or investigation of a biochemical or serologic character.

The ringworm fungi are extremely sensitive to slight differences in culture medium, and, as cultures are often secured only as a result of considerable effort, they should be made under conditions that render them of maximum value toward establishing their correct classification. Greater uniformity in the use of Sabouraud's methods and cooperation and standardization of details of technic would be very desirable among those interested in making greater progress in this work, and in this way it is believed that some of the uncertainties that have hampered,

in many cases, the positive identification of species would be lessened. It is hoped that this preliminary report may, by affording opportunity for exchange of cultures and ideas, be helpful to some extent in eliminating some of these difficulties.

II. HISTORICAL SURVEY

The literature regarding onychomycosis has not until within recent years presented any cultural proof as to the nature of the fungi causing the disease. The affection is generally considered as one of great rarity, and while it is recognized as being caused by both *Trichophyton* and *Achorion*, the relative frequency of ringworm and favus of the nails has been a matter of some doubt.

While unaccompanied by any record of cultures, the paper of Foster,¹ containing observations on the prevalence of onychomycosis among aliens arriving at Ellis Island during a period of eight months, is of much interest. He states that:

In our series of 101 cases, eighty-four were ringworm and seventeen favus. This would indicate that ringworm is encountered about five times as often as favus. It is also interesting to know that these 101 cases were discovered among 521,366 aliens who were examined. Roughly speaking the ratio of cases was about one to five thousand of these foreigners.

Sabouraud was formerly of the opinion that, of *Trichophyton*, only the endothrix varieties attacked the nails. The frequent failure to secure cultures led him to believe that some undescribed species might be largely responsible. Sabouraud² notes the rarity of this affection in Paris, having observed only two cases among 500 cases of ringworm affections that were the object of special study by him.

While the conclusions of Sabouraud that each species of the ringworm fungi tends to produce always a special clinical type of the disease has provoked much discussion and difference of opinion, the fact remains that with some exceptions, the statistics presented by him and others in main bear out his contention. The species of *Microsporon* are not accredited with attacking the nails, but they and the endothrix trichophytons are responsible for practically all cases of scalp ringworm. The ectothrix trichophytons, especially the large-spored variety, rarely attack the scalp, but are responsible for many of the beard cases of ringworm.

The epidermophyton, which is so largely responsible for tinea cruris and certain eczematoid eruptions of the hands and feet that have attracted the attention of dermatologists of recent years, is not generally considered as either attacking the hair or nails.

1. Foster, Milton H.: Favus and Ringworm of the Nails, J. A. M. A. **63**: 640 (Aug. 22) 1914.

2. Sabouraud: Les Teignes, Paris, 1910.

That climate, which is recognized as an important factor in many of the ringworm affections, may exert an influence in the nail affection is suggested by the observations of Castellani and Chalmers³ in Ceylon:

Cases of tinea unguium or onychomycosis occur in the tropics and are generally due to the same fungus producing dhobie itch, both epidermophytos and trichophytos. The nails of the fingers as well as of the toes may be affected. Tinea unguium may be caused also by the fungi of the genus endodermophyton, the nails being often affected in tinea imbricata.

That the limited number of cases of which cultures have been reported, with the exception of favus, were caused by both endothrix and ectothrix trichophytos of the large-spored variety, has been shown by the cultural work of Sabouraud, Ravogli, Dalla Favera and Low.

Ravogli⁴ in this country reported cultures from two cases—one not associated with ringworm in any other portion of the body and another case associated with ringworm of the scalp due to megalosporon of the endo-ectothrix variety. The same fungus was obtained in cultures from both the scalp and affected nails.

In Italy Dalla Favera,⁵ of six cases of onychomycosis, reports five as due to *Trichophyton violaceum* (endothrix) and one due to *Trichophyton rosaceum* (ectothrix).

Low,⁶ in Scotland, reports nineteen cases with cultures from eight cases, two due to *Trichophyton rosaceum*, five due to *Trichophyton cratiforme flazum* (endothrix) and one due to an unknown fungus. One of these cases was contracted by the mother from a child with ringworm of the scalp. The sources of infection in the other cases were not determined. With two exceptions, the patients were females and were exposed to a possible source of infection in washing clothes. Low notes that Vidal observed that nurses who epilated ringworm cases at the hospital Saint Louis in Paris frequently became infected with ringworm of the nails.

In this country, Lane⁷ reports a case in which the nail affection was continuous with the eruption on the fingers.

3 Castellani and Chalmers: Manual of Tropical Diseases, Ed. 3, London, William Wood & Co., 1920, p. 2059.

4. Ravogli, A.: Onychomycosis Trichophytina, With Report of Two Cases, J. A. M. A. **49**:308 (July 27) 1907.

5. Dalla Favera, G. B.: Sur l'état actuel des trichophyties de la province de Parme (Italie), Ann. de dermat. et syph., 1909, p. 433.

6. Low, R. Cranston: Fungus Infections of the Finger Nails, Edinburgh M. J. **6**:121 (Feb.) 1911.

7. Lane, J. E.: Ringworm of the Hands and Feet, Boston M. & S. J. **174**: No. 8 (Feb. 24) 1916.

The frequently quoted paper of Ormsby and Mitchell⁸ has directed attention to the prevalence of the affection studied by them in this country. That this condition may, with the possible exception of those caused by the epidermophyton, involve the nails, lends additional interest to the study of these cases and the frequently coexisting affection, *tinea cruris*.

That other fungi may attack the nails has been reported by Brumpt and Langeron; Weil and Gaudin have also reported cases of onychomycosis in which *Penicillium brevicaula* was found. As is not unusual in nail cases, several other species of molds were found. Their work is reviewed by Weidman⁹ in a paper reporting the finding of this fungus for the first time in a case of onychomycosis in this country. As the inoculation of monkeys and human beings was unsuccessful, Weidman is somewhat doubtful of its pathogenicity.

HISTORY OF CASES

Sixteen cases of onychomycosis are embraced in this report. The presence of a fungus of the trichophyton type has been established in every case by a microscopic examination of the nail parings.

The fact that the majority of these cases were found in a small city of 12,000 inhabitants, several being among acquaintances, indicates a prevalence considerably greater than reported by Foster of one to 5,000 among immigrants at Ellis Island. Exact statistics are not available, but the inclusion of several cases, not embraced in this report, but observed by local physicians, would indicate a ratio of at least one case to each 500 of population—a prevalence ten times greater than reported by Foster among foreign immigrants. These cases, to a large extent, represent a special class, among them being included a physician, a lawyer and professors, American-born people who bestow more than ordinary care on personal cleanliness. It is noteworthy that no case was found due to *favus* and none to fungi other than trichophytons of species apparently seldom responsible for scalp ringworm but specifically inclined to attack the nails.

The history of several of these cases indicates a rather wide distribution of the species of which cultures have been obtained in twelve cases and may indicate climatic conditions rather than species as being a factor in the prevalence of the affection. One case was apparently contracted while the patient was living in Cuba, another case was

8. Ormsby, O. S., and Mitchell, J. H.: Ringworm of the Hands and Feet, J. A. M. A. **67**:711 (Sept. 2) 1916.

9. Weidman, Fred D.: *Penicillium Brevicaule* Var. *Hominis* Saccardo, 1877, Brumpt and Langeron, 1910, in an American Case of Ringworm of the Toes. Arch. Dermat. & Syph. **2**:703 (Dec.) 1920.

thought to have been contracted by a student in Germany, and a third case had existed for several years previous to the patient's removal from New York.

The invasion of the nails was in every case reported to be secondary to an eruption on the hands or feet which coexisted with the nail affection and was of varying degrees of severity. In one instance the



Fig. 1 (Case 1).—Trichophyton "A"; for thirty-five years the skin and all the nails of the right hand and of the feet were affected with ringworm. The photographs were taken after partial and complete cure with Whitfield's ointment.

foot trouble was reported to have confined the patient to bed for several days. In the majority of the cases ringworm of the thighs was either present or was reported to have been present at some time.

With one exception, all of the patients were men, one woman having contracted the skin infection, followed by nail infection, from

her husband. With three exceptions, the toenails were first involved. In seven cases the toenails only were affected; in five both toenails and fingernails, and in four cases only the fingernails. The infection of the fingernails was more frequently confined to the right hand.

In one case (Fig. 1) all five nails of the right hand had been affected for about twenty-five years before the affection extended to the left hand, its appearance on this hand being first noticed as a small papule, itching intensely, and slowly enlarging in a circle. After several months it extended to, and involved, the thumb nail. The invasion of the nail seemed to be dependent on some slight injury as the affection was observed to remain confined to the finger end for some time before



Fig. 2 (Case 11).—*Trichophyton* "B"; condition of nails of several years' standing due to ringworm; skin of feet slightly affected; hands markedly so, causing much discomfort during cold weather.

there was any evidence of the nail being affected, and was first noted as a slight soreness as if the nail plate had been torn loose slightly.

The infection always began at the free margin of the nail and slowly undermined the nail plate until it became so loosened that it was either shed or removed by trimming. Subsequent growth showed a thickened nail of worm-eaten appearance, more or less irregular and of a dirty yellowish color, the outgrowing diseased nail plate often being shed at intervals of a few months. In some cases the invasion of the fungus under the nails did not progress more rapidly than the growth of new nail and only one half or less of the nail would be affected, a condition often extending over several years.

An outstanding feature of these cases, in contrast to many of the European observations, is that no member of the family or associates, so far as known, was affected with ringworm of the scalp, although young children susceptible to scalp ringworm were constantly exposed to infection. In one case the nail affection had existed since the age of 5 years, three other members of the family being similarly affected with ringworm of the hands and feet involving the nails. The entire absence of a history of scalp ringworm would seem to exclude the probability of *endothrix trichophyton* as a cause. The character of the species in Case 1 is indicated by its disposition to attack the hair follicles on the back of the hand at times causing considerable irritation. There is some evidence in this case that a mild type of ringworm of the beard, consisting of somewhat scattered scaly areas, confined mostly to the under part of the chin, had been present at times, but had readily yielded to applications of mild parasiticide ointments.



Fig. 3 (Case 6).—*Trichophyton gypsum*, variety "C"; ringworm of the toe nails and feet of several years' standing, following a severe attack of beard ringworm. Cultures from the nails show a trichophyton of the gypsum group. The partial invasion of the nails, shown here, which is somewhat further advanced than indicated in the photograph, is not peculiar to this case or species, as in several other cases caused by a different species the invasion of only the free margin of the nails was prolonged through a period of several years; usually the progress of the disease is more rapid, completely undermining the nail plate which is shed or removed by trimming. Subsequent growth shows the characteristic thickened nails of a yellowish and worm-eaten appearance.

A physician (Case 6) gave a history of beard ringworm of the suppurative type previous to the nail affection, several cases of this type of beard ringworm having apparently originated from the same barber shop. The fungus in the nail was found by cultures to belong to the gypsum group, a variety noted for producing the severer type of beard ringworm. The beard condition had been cured at the time of examination of the nails.

Except for the family infection of the same nature, none could be traced to any other source either human or animal.

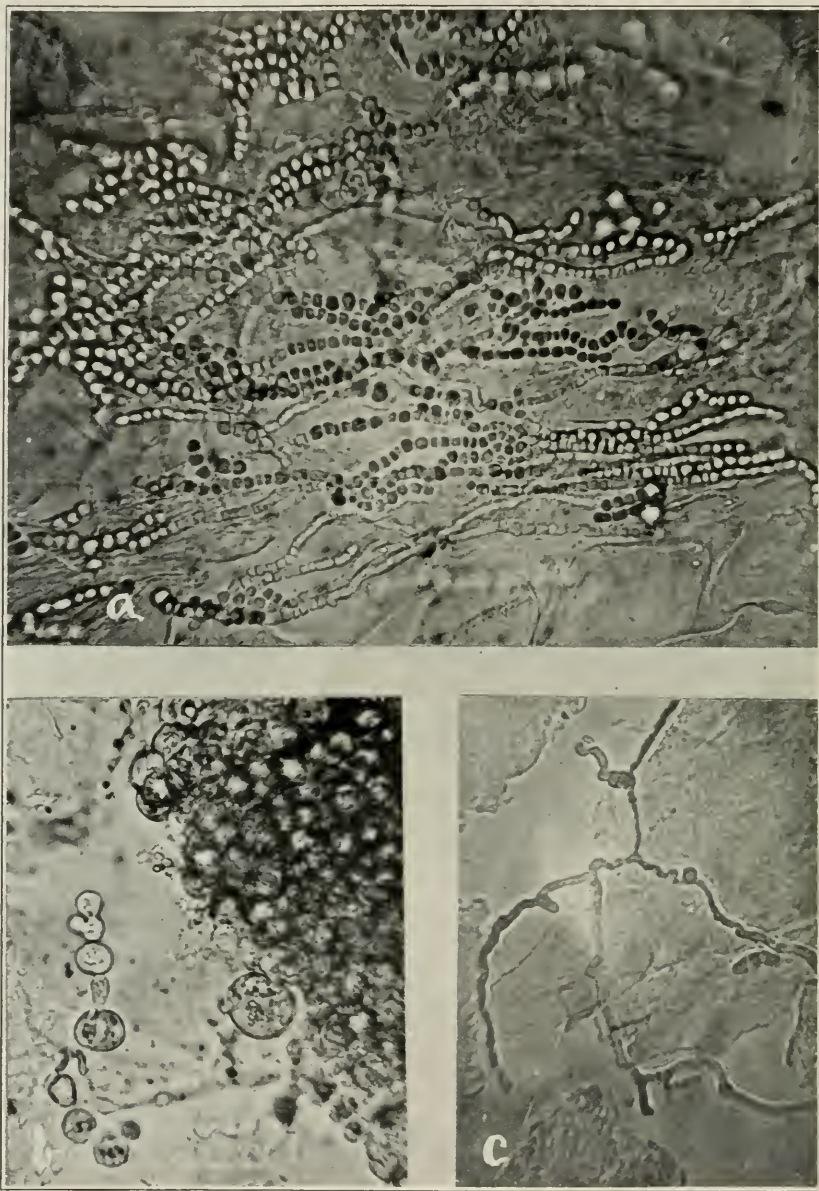


Fig. 4.—Trichophyton "A." Appearance of fungus in potash preparations of affected nail parings; *a*, Case 3, showing sporulated and nonsporulated mycelium and free spores; *b*, Case 12; in addition to the fungus similar to *a*, unusually large spores suggesting a different species were present in large numbers; however, only cultures of Trichophyton "A" were obtained; *c*, Case 1. In nail parings the mycelium is often irregular and knotted in appearance. ($\times 500$)

MICROSCOPIC EXAMINATION

The importance of a thorough microscopic search for the fungus has been emphasized in recent years by the not unusual confusion of some of the ringworm affections with other skin diseases. Even syphilis has shared in this confusion, and cases are on record as being so diagnosed and treated. That forms of onychia, presenting many of the characteristics of ringworm, may be caused by eczema, psoriasis or syphilis, increases the importance of a thorough search for the fungus.

The finding of the fungus in nail parings is generally considered somewhat more difficult than in the hair or skin. Much depends on a suitable selection of parings. In the series of nail cases studied, the fungus could be found without undue difficulty when a more or less affected nail plate remained showing on the under surface a granular or fibrous character. When the entire nail plate had been cast or kept closely trimmed, much greater difficulty was experienced in finding the fungus.

The preparation of material is made in the usual way. Bits of pinhead size are treated on a glass slide with a 10 to 20 per cent. solution of potassium hydroxid gradually heated to the boiling point and allowed to cool. After a lapse of time, varying from a few minutes to several hours, depending on the size and hardness of the parings, the material is so softened that pressure applied to the cover glass will spread the material in a thin smear. Examination is made with a 4 mm. objective.

In this series of cases I have been unable to establish any correlation between the appearance of the fungus found in the parings and the three groups of cultures obtained. In the nails both simple and sporulated mycelium and frequently free spores were found. Owing probably to the harder nail structure, the mycelium frequently assumes knotted and distorted forms.

The appearance of the fungus in Case 12 (Fig. 4b) is rather unusual and suggests the presence of a different fungus, although several cultures of species designated temporarily *Trichophyton "A"* were obtained. In addition to the usual simple and sporulated mycelium, masses of large spores of as much as 20 microns in diameter filled with granular matter were present in large numbers. Fresh parings examined one year later exhibited the same characteristics. The appearance in some ways suggests *Penicillium brevicaulis* found by Weidman in an American case of onychomycosis. I hope to make a further study of this case.

On two occasions in Case 1 (Fig. 5) from lesions on the thighs I have found lanugo hairs surrounded by the fungus, mycelium and free spores about 4 microns in diameter being present. The invasion

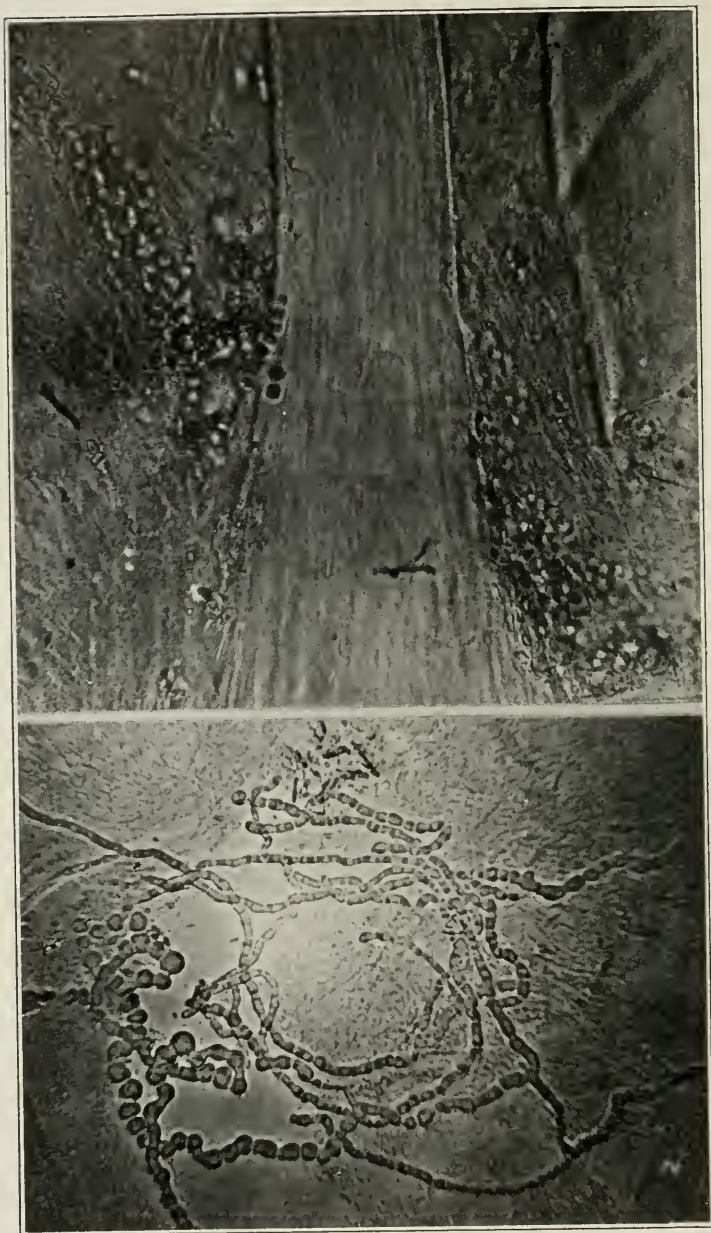


Fig. 5 (Case 1).—Trichophyton "A"; *a*, portion of lanugo hair from thigh showing fungus; *b*, fungus as found in skin of thigh lesions. *Tinea cruris* coexisted with the nail affection in several cases. ($\times 500$)

apparently had not extended beyond the stage of invasion of the hair follicle, the fungus apparently being of the large-spored ectothrix variety.

A guinea-pig inoculated from a culture of Case 1 nail gave a scaly reddened area in which on the eighth day the fungus was found; however, no evidence of affected hairs was found. The infection showed signs of curing on the fifteenth day, and was entirely well by the twentieth day.

Further study of this feature is contemplated by animal inoculations and the possibility of finding the fungus in scalp, beard or animal cases.

CULTURE MEDIUMS

The desirability of using mediums prepared with the peptone and maltose or glucose proposed by Sabouraud as international proof medium is unquestioned if any satisfactory comparison of species is to be made with those described by him. Owing to my inability until recently to secure a supply of this material, I was forced to use in my first cultural work such peptone and maltose as were available. First Witte and later Difco peptone was used. That the maltose from several sources was of approximate purity was indicated by its specific rotary power being from $[\alpha]_D = 120$ degrees to $[\alpha]_D = 130$ degrees and comparative absence of dextrin; the specific rotary power of pure hydrated maltose being $[\alpha]_D = 132$ degrees. Mediums in all other respects were prepared in accordance with Sabouraud's formulas for proof medium. Cultures were grown with the idea that they might be classified into groups and later representatives of each group studied on Sabouraud's proof medium whenever that was obtainable. This has been facilitated through the kindness of Dr. Highman of New York in providing me with a small amount of Sabouraud's culture material. More recently I have secured a supply from Cogit & Cie, Paris. That it is the standard proposed is indicated by the labels; "Maltose brute" and "Glucose masse du Docteur Sabouraud." In addition to the two crude sugars a supply of Chassaing peptone and filter paper (papier Chardin) was obtained. Merck's shred agar of sufficient quantity for the other material was obtained in this country. Partial analyses of the Sabouraud maltose and glucose have been made with the purpose of being able to establish more certainly their identity with other lots that might be secured from other sources. The glucose is light yellow and the maltose very dark brown, affording mediums of corresponding color. Both are practically free from matter insoluble in water. Filtration of medium through the filter paper afforded a medium somewhat clearer than that filtered through cotton.

It is rather surprising to find these two crude sugars of very much the same composition. Both, according to American standards,¹⁰ would be classed as crude dextrose, the term glucose being restricted to syrupy products. Maltose is a relatively minor constituent even in the Sabouraud maltose. This is indicated by their specific rotary power of $[\alpha]_D = 51$ degrees for the glucose and $[\alpha]_D = 52$ degrees for the maltose, pure anhydrous dextrose being $[\alpha]_D = 52.7$ degrees. As these crude sugars are not anhydrous but contain 12 to 15 per cent. water and are comparatively free from dextrin, a small amount of maltose is indicated. Different lumps varied slightly, suggesting the desirability of breaking up and mixing. Their similarity of composition is further indicated by the practical identity of cultures on the two mediums and the absence of a hygroscopic quality in the Sabouraud maltose so characteristic of maltose. That this supply of Sabouraud maltose agrees in composition with that obtained from Dr. Highman is further proof that it is genuine. As the material is accepted as a standard, these tests are of little importance except as showing that in the use of substitutes of approximately pure maltose how far the departure is from the proof medium of Sabouraud. On account of the light color of the medium, permitting examination more readily from the back, the Sabouraud glucose would seem to offer some advantages over the maltose. As a substitute, a medium prepared with American dextrose (technical) and Difco peptone approached most nearly the Sabouraud maltose in appearance of cultures.

CULTURES

Material for cultures is selected with regard to that richest in the fungus, as shown by the microscope. Reduced to bits, pinhead size or smaller, it is treated for two or three minutes with alcohol to inhibit the growth of bacteria, and plants are made on slants, three or four to the tube. A common sewing needle fused in the end of a glass tube serves admirably for making the transfers. At least fifty plants are usually made, as in poorly selected material many fail to develop and some are overgrown with bacteria and more rapidly growing common molds. In extreme cases only one culture was obtained from fifty plants. Frequently, with good selection, as many as one half develop. With these cases growth was often noticeable as early as the third or fourth day, and the culture was transplanted to a larger flask to provide sufficient room for development. Cultures were maintained at room temperature, except during cold weather when they were incubated at

10. Rogers, Allen: *Manual of Industrial Chemistry*, Ed. 2, New York, D. Van Nostrand Company, p. 772.

about 25 C. The appearance of the cultures was most characteristic in from three to six weeks, development being noticeably more rapid during the summer.

Microscopic morphology was studied by drop cultures prepared according to Sabouraud, and by Klatsch preparations.

The use of gentian-violet¹¹ in proper dilution for restraining the growth of gram-positive bacteria offers much toward simplifying the procedure of obtaining pure cultures. The possible influence of this or alcohol on the morphology of these molds should be considered; however, one set of cultures obtained after cleansing the skin with water and another set in which alcohol was used did not differ perceptibly.

While cultures from this series of cases have certain characteristics agreeing with some of Sabouraud's species, certain differences suggest new species, and it is deemed best to defer their definite classification until more extended comparative study can be made with Sabouraud's type cultures.

The three species of trichophytons found in these twelve cases are temporarily designated: Trichophyton "A," Trichophyton "B" and Trichophyton gypsum, variety "C."

Trichophyton "A": Seven cases—1, 2, 3, 5, 12, 13 and 14. Cultures on Sabouraud's proof maltose agar were snow-white at first but usually showed a pink color after three weeks. The color from the back was violet to purplish red, depending apparently on the depth of medium. Cultures grown in flasks were usually divided by radial furrows. Old cultures after several weeks became covered with a white pleomorphic growth. Drop cultures showed conidiophores both simple and branched bearing pyriform conidia (spores) and pluriseptate fuseaux of characteristic slender form, the extent of their formation apparently being influenced by the drying of the culture. Cultures on peptone agar showed a white central duvet, sometimes tinged with pink, surrounded by a smooth portion devoid of duvet. The macroscopic appearance of cultures from different cases of this group showed some variations in amount of duvet and development of pink color.

Trichophyton "B": Four cases—7, 11, 15 and 16. Cultures on Sabouraud's proof maltose agar were of a pronounced white downy type at first, later showing a slight yellowish coloration in places. The color from the back was usually slightly yellow. Drop cultures showed unbranched conidiophores, not very abundant, bearing pyriform conidia (spores). No fuseaux were observed. Cultures on peptone agar were partially covered with a white down, slightly yellow from the back. Sub-cultures frequently showed a purple color from the back and white

11. Farley, David L.: The Use of Gentian-Violet as a Restrainer in the Isolation of the Pathogenic Molds, *Arch. Dermat. & Syph.* **2**:459 (Oct.) 1920.

surface down later becoming pink. Some of the characteristics suggest *Trichophyton equinum* but others, especially subcultures, suggest a possible pleomorphic relationship to the first group. * The cultures from the different cases were more constant in their appearance than those of the first group.

Trichophyton gypsum, variety "C": One case—6. This was a rapidly growing culture, growth frequently being noticeable as early as the second day. On Sabouraud's proof maltose agar the culture was first white, becoming cream color. The diameter of the culture may reach 10 cm. by the thirtieth day. Cultures on peptone agar were slightly yellow from the back and covered with a white down, later showing a light cream color. Drop cultures showed conidiophores, frequently in clusters, bearing pyriform nearly oval conida and rather short fuseaux and numerous spirals characteristic of the *gypsum* group.

The cultures from the different cases represented by *Trichophyton* "A" have some minor differences, the extent of which is not strictly comparable, as several cases were studied on mediums prepared with different peptones and sugars. Case 1 of this group has afforded opportunity to study this species in various mediums from plants of fresh parings. Cultures frequently on the third or fourth day, especially during the summer, show signs of growth, first as a small white tuft increasing slowly in diameter, the outer portion often remaining free from down during the first two weeks. From the back, when about two weeks old, they usually show a violet tending toward a purplish-red if grown in a thin stratum of medium. The possible influence of alteration of hydrogen-ion concentration of the medium by drying or otherwise might afford some explanation of these variations of color, as well as other differences in cultures. Cultures grown on Difco chemically pure maltose and Difco peptone presented entirely different characteristics, being practically free from duvet, violet or pink coloration, and the edges presented a rayed appearance. Other less pure samples of maltose gave a violet color from the back and slight duvet. Difco peptone, with dextrose (technical), afforded characteristic cultures similar to those on Sabouraud maltose or glucose agar with perhaps a tendency to a more decided pink color. Cultures on peptone agar using Difco brand were similar to those obtained with Chassaing peptone. In some tube cultures, especially in the lower part of the tube where moisture is greater, some peptone cultures remained entirely free from duvet (Fig. 6f). Peptone cultures are of a light orange color from the back with no suggestion of the dark center noted by Sabouraud as characteristic of *Trichophyton rosaceum*, with which this species might be confused.

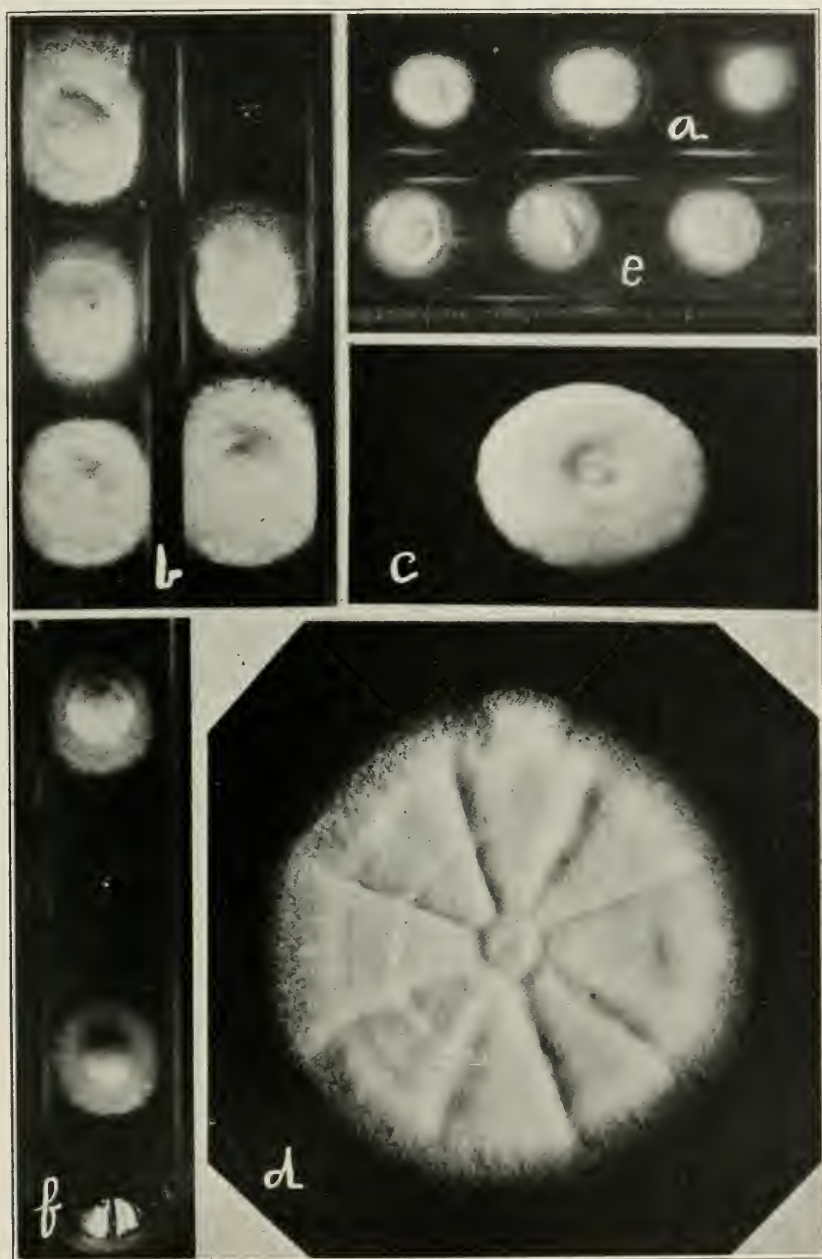


Fig. 6 (Case 1).—Nail, *Trichophyton* "A"; *a*, tube cultures on Sabouraud's maltose agar two weeks old; *b*, tube cultures three weeks old; *c*, flask cultures three weeks old; *d*, flask cultures six weeks old; *e*, tube cultures on peptone agar two weeks old; *f*, tube cultures on peptone agar three weeks old.

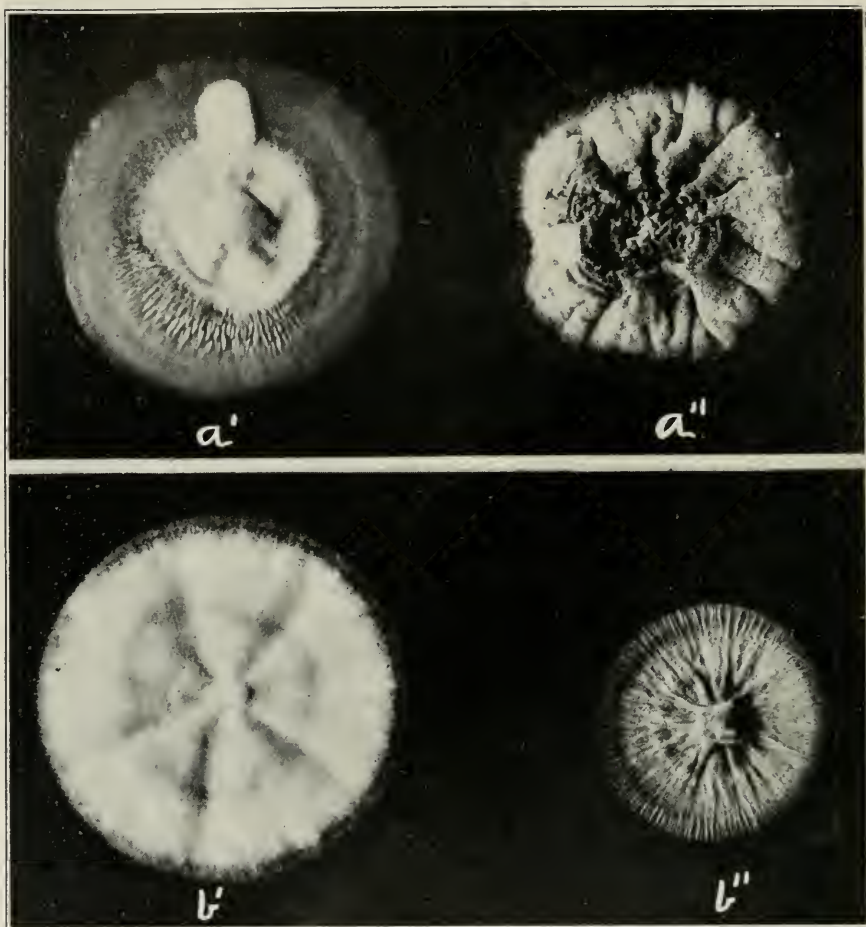


Fig. 7 (Case 1).—Trichophyton "A"; variation in primary cultures from nail and thigh lesions of the same case grown in the same culture flask; *a'* and *a''*, thirty-day old cultures on Sabouraud's peptone agar; *a'* from nail, duvet slightly pink; *a''*, from thigh, orange colored culture; *b'* and *b''*, thirty-day old cultures on Sabouraud's maltose agar ("Maltose masse du Docteur Sabouraud" and peptone Chassaing); *b'*, from nail central area pink; *b''*, from thigh, scanty duvet of purple color. These differences are lost to a great extent in subcultures, showing the close relationship of the cultures from the two lesions. This is further confirmed by the microscopic morphology of the two cultures.

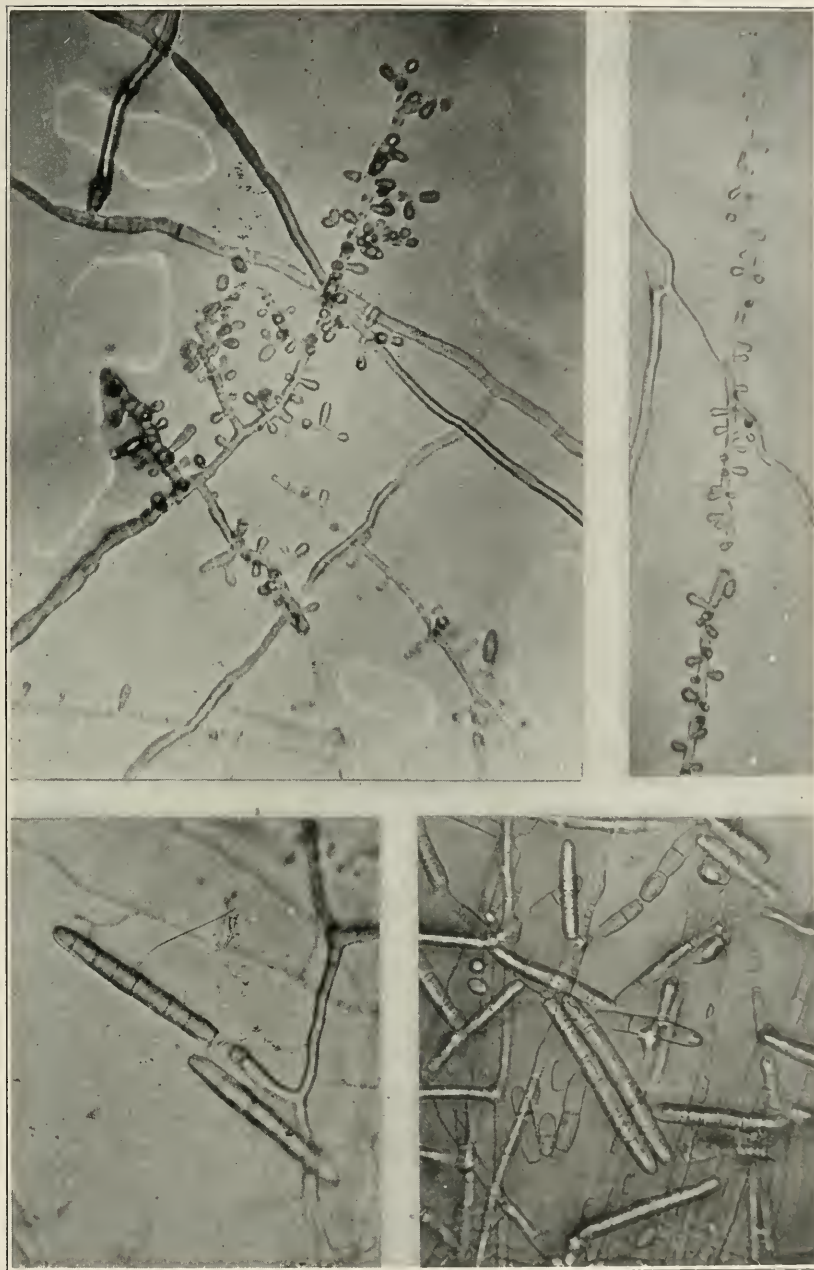


Fig. 8 (Case 1).—*Trichophyton* "A": conidia and fuseaux in hanging drop cultures on Sabouraud's maltose bouillon. ($\times 500$)

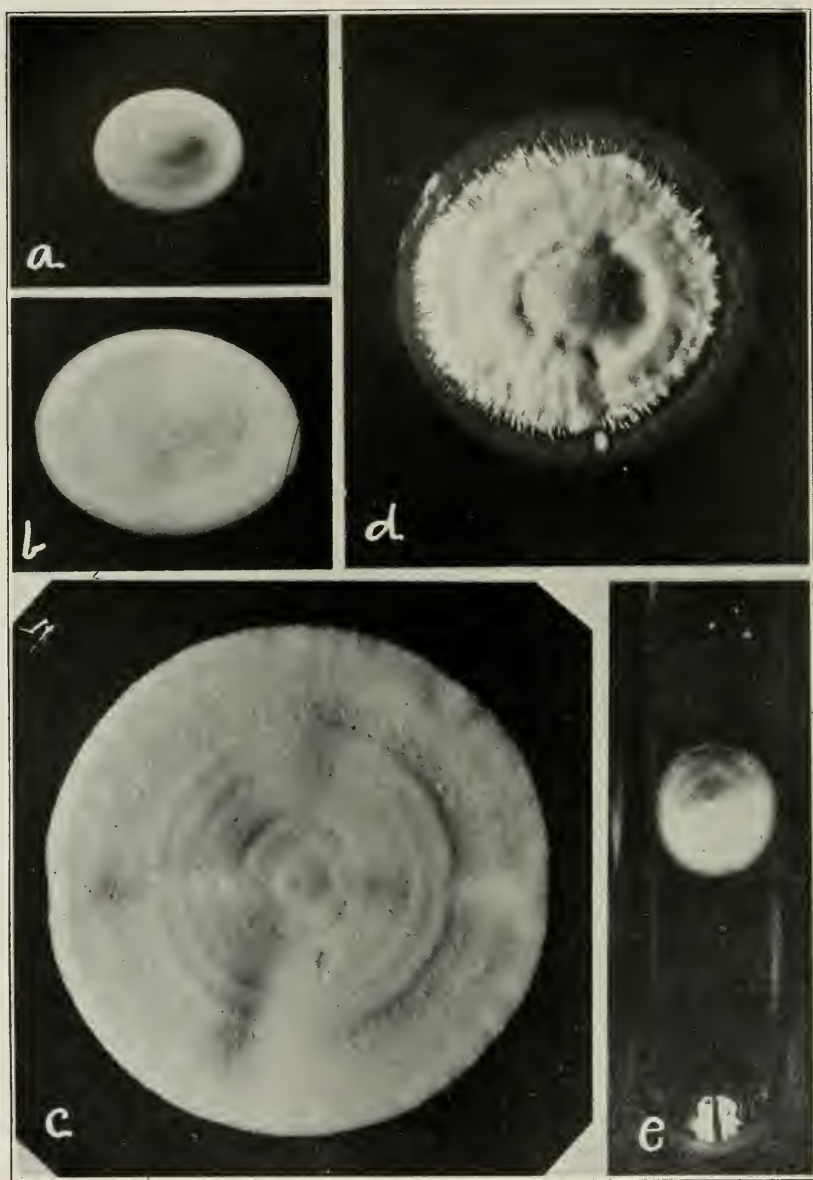


Fig. 9 (Case 11).—*Trichophyton* "B"; Cultures *a*, *b* and *c* on maltose agar ("Maltose masse of Dr. Sabouraud" and peptone Chassaing): *a*, three weeks old; *b*, four weeks old; *c*, six weeks old; *d*, six-week old culture on peptone agar; *e*, tube culture three weeks old on peptone agar.



Fig. 10 (Case 6).—*Trichophyton gypsum*, variety "C"; culture three weeks old on peptone agar (peptone Chassaing 3 per cent.).

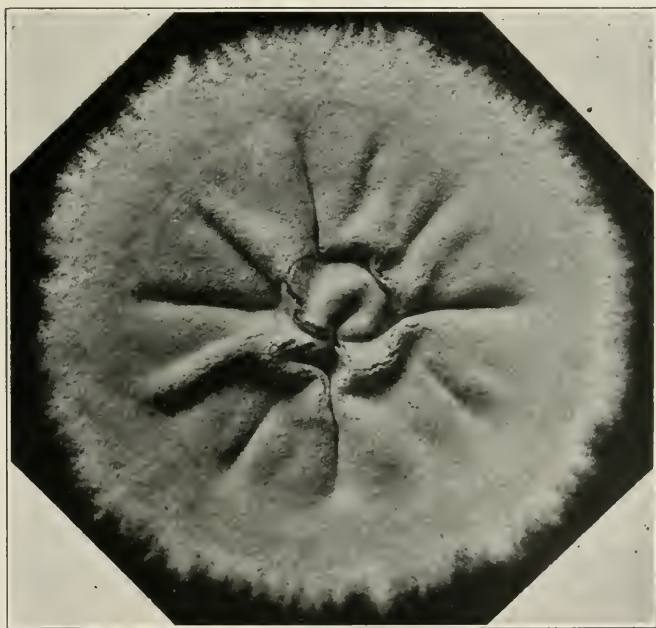


Fig. 11 (Case 6).—*Trichophyton gypsum*, variety "C"; culture four weeks old on maltose agar ("Maltose masse du Dr. Sabouraud" and peptone Chassaing).

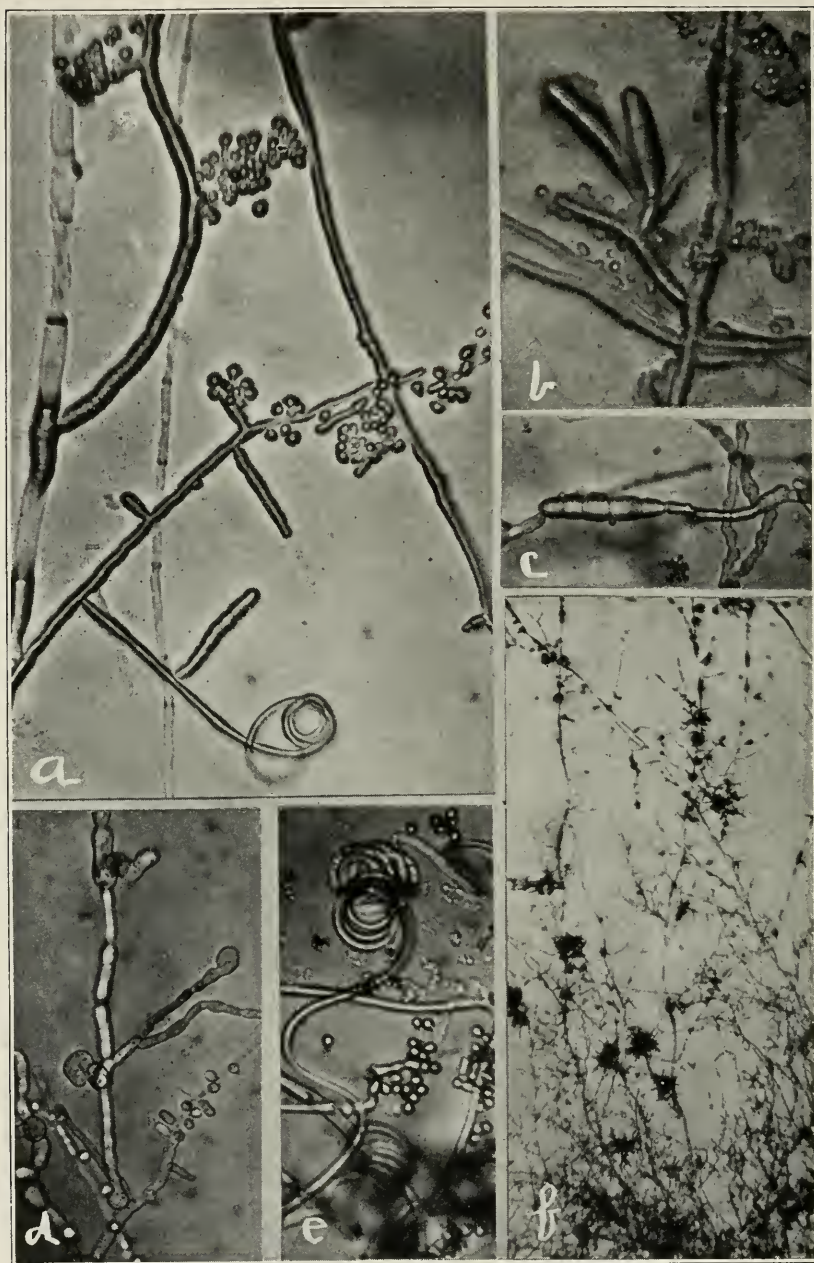


Fig. 12 (Case 6).—*Trichophyton gypseum*, variety "C"; drop cultures on Sabouraud's maltose bouillon; *a*, *b*, *c*, *d* and *e*, conidia, fuseaux spirals and nodular bodies, $\times 500$; *f*, spore clusters characteristic of gypseum group, $\times 50$.

Microscopically, the fuseaux, as found in drop cultures of this species, are especially characteristic and would seem to distinguish it from *Trichophyton rosaceum*. These fuseaux, of characteristic slender form, are borne on sides and ends of conidiophores in the same manner as the conidia, and while they are abundant usually in drop cultures, they are less frequently observed in tube cultures, and have been noted only on two occasions in Klatsch preparations from flask cultures.

VARIATIONS IN CULTURES FROM THE SAME CASE

The coexistence of tinea cruris with the nail affection in Case 1 has afforded a convenient opportunity to study cultures from two lesions of different character in the same case. The differences noted, as well as their occurrence in similar cases, are being further investigated, but it is believed that they merit at this time a rather detailed notice. Wende and Collins,¹² in a recent paper, have noted a somewhat similar condition in which two types of epidermophyton were found in the same lesion.

It was observed that the primary cultures from the thigh and nail lesions of the patient in Case 1 presented rather striking differences and, to make the comparison under more nearly identical conditions, primary plants have been grown side by side in the same flask, using a one-quart Blake bottle laid on the side, providing in this way a surface of medium about 9 by 20 cm. and 1 cm. in depth. Scrapings from both lesions were treated with alcohol in the same way to kill bacteria and planted the same day in tubes. As soon as growth was noticeable, usually on the fourth or fifth day, they were transferred to the same flask. Precautions were taken to make the plants of the same depth in the medium and to transfer the whole culture, and, except for possible difference in preliminary treatment, which seemed improbable, the identity of conditions was assured.

The cultures from the thigh (Fig. 7*b*) showed less development of duvet on the maltose agar; both showed purplish red from the back. Microscopically both showed fuseaux characteristic of *Trichophyton* "A" but these fuseaux were more abundant in the cultures from nail. On peptone agar cultures from the thigh were of a more pronounced orange. Subcultures lost these characteristics to some extent and confirmed the close relationship of the cultures, but, as in no case have they been cultivated beyond the third transfer, the persistence of these differences is not known. These differences have not been entirely regular, varying somewhat at different times, and while the growth of one culture would be true to previous type, the other in the same flask

12. Wende, Grover W., and Collins, Katherine R.: A Contribution to the Study of Epidermophyton Inguinale, Arch. Dermat. & Syph. **3**:1 (Jan.) 1921.

would show a variation. The purity of the cultures seemed beyond question, and was indicated by growth of cultures from apparently a single spore by dusting a fragment of a culture over the surface of the medium, numerous cultures free from any appearance of contaminants developing.

To whatever these differences may be attributed, environment or technic, the persistence with which they have appeared in numerous sets has caused much perplexity; they afford a striking example of the pleomorphism to which the trichophytons are subject and which is a source of so much confusion in identifying species.

The diverse character of some of the skin lesions of ringworm, caused by the same species, might suggest the idea of a symbiotic relationship of these fungi with some of the various common saprophytic molds or bacteria so often associated with them in lesions. Stitt¹³ refers to such a symbiosis between a fungus and a coccus found in cases of *dhobie itch*. Opposed to this possibility, as being general, is the successful inoculation with pure cultures by Sabouraud and others, reproducing many of the characteristic types of ringworm affections in human beings and animals.

TREATMENT

It is with some degree of diffidence that, as a layman, I refer to treatment; but, owing to the rather unusual opportunity afforded to appreciate the cure of an annoying affection of many years' standing, I am persuaded that a brief statement will not be without interest to the reader.

For thirty-five years the patient in Case 1—the true nature of whose disease had not been recognized—had been treated with various applications with little improvement, except to allay somewhat from time to time the severity of the eruption on the hands and feet. Following a demonstration of its true nature, several forms of treatment were tried, among them soaking the nails in a solution of mercuric chlorid followed by application of ammoniated mercury ointment. No improvement of the nails was noted after about two months of such treatment. Roentgen-ray treatment was not tried in this case, but in two other cases of this series a few exposures had been given without apparent improvement.

A trial of Whitfield's ointment—benzoic acid 4 parts, salicylic acid 2 parts, petrolatum 30 parts—was prompted by the success reported by Ormsby and Mitchell attending its use in treatment of ringworm of the hands and feet. The immediate effects of this ointment after a few days' use were so pronounced and favorable on the skin eruption that

13. Stitt, E. R.: *Practical Bacteriology and Blood Work*, Ed. 6, Philadelphia, P. Blakiston's Son & Co., 1920, p. 178.

attention was directed to the nails. In order to reach the fungus, it was found necessary to scrape the nails repeatedly after applying a solution of potassium hydroxid of about 10 per cent. strength. Whitfield's ointment was applied at night, being held in place on each nail with a small piece of cloth and narrow strips of adhesive cloth. Whatever adhesive matter from the cloth remained was easily removed the next morning with a cloth and a little gasoline. Treatment, although productive of some inflammation, interfered in no way with daily duties. If irritation became too severe, use of the ointment was discontinued for a few days or else it was diluted considerably with petrolatum. Successful destruction of the fungus was in several instances accompanied by some pus formation under the diseased nail bed. Partially invaded nails gave more trouble than when the entire nail was involved for, in spite of close trimming, the fungus would apparently always have invaded some place a little farther back under the nail plate than could be reached by the ointment, and it was only after trimming well back of the infected portion that success was attained.

Owing to the possibility of keeping the ointment more constantly in contact with the toe nails, it was not found necessary to use the potash solution, as the application of the ointment softened the nail sufficiently for the removal of the affected part by close trimming.

With this persistent treatment, improvement was soon noted and within about four months the finger nails had attained their normal growth. The toe nails required a somewhat longer time to grow out. There has been no reinfection of the finger nails after a lapse of two years, but two of the toe nails after several months showed some reinfection requiring further treatment.

Another case in which this ointment was markedly effective was that of the patient in Case 7, a cure of all the nails of the right hand being attained after several months' use of the ointment following persistent scraping.

Several other patients have shown improvement as evidenced by one or more nails becoming normal, and with such encouragement more persistent treatment will probably effect a complete cure. In several cases the beneficial effects of the ointment on the skin eruption has afforded great relief. Some of the more callous places on the hands resisting penetration of the ointment have been removed more easily by the application of the potash solution somewhat diluted.

It is unquestionably true that a large part of the difficulty in curing ringworm of the nails as ordinarily treated by the physician is due to the difficulty of getting the patient to persist in any treatment that is

necessarily slow at best, and the success of which is so dependent on the personal efforts of the patient. Low, referring to treatment with various applications, states: "To get a good result the patient must be seen frequently and the nails scraped by the doctor himself." While such attention on the part of the physician may often be impracticable, it is difficult, without frequent supervision and encouragement from a physician, for the average person to appreciate the thoroughness of scraping and the persistence in applying the ointment that are so necessary to effect a cure. Consequently a disease that should present no particular difficulty of cure is perhaps in the majority of cases allowed to continue through life.

SUMMARY AND CONCLUSIONS

The conclusion is reached, based on the work presented in this paper, that onychomycosis is far more prevalent, especially in the southern part of the United States, than is generally recognized, and that large-spored ectothrix trichophytons are largely responsible for the affection. A conservative estimate would indicate a ratio of at least one case to each 500 of population, a prevalence ten times greater than reported by Foster among foreign immigrants at Ellis Island.

Of the sixteen cases of onychomycosis observed, cultures have been obtained in twelve of the thirteen cases in which cultures have been attempted at the time of making this report. The entire absence of a history of ringworm of the scalp associated with any of these cases would, it is believed, exclude the probability of endothrix trichophytons as a cause. That eleven of these cases were caused by large-spored ectothrix trichophytons is indicated by finding in associated skin lesions lanugo hairs attacked by a fungus apparently of this variety. This conclusion is further strengthened by their rapidity of development on culture mediums and other cultural characteristics.

The species, pending their more definite classification, are designated as Trichophyton "A," Trichophyton "B" and Trichophyton gypseum, variety "C."

Trichophyton "A" (seven cases) produces white downy cultures on Sabouraud's maltose agar, usually showing a pink color on the surface and purplish red from the back. Drop cultures show pyriform conidia borne on simple and branched conidiophores, and more rarely characteristic slender fuseaux.

Trichophyton "B" (four cases) produces on Sabouraud's maltose agar pronounced white downy cultures, tinged with yellow as they grow older. Drop cultures show pyriform conidia, not very abundant.

Trichophyton gypseum, variety "C" (one case) produces on Sabouraud's maltose agar rapidly growing white downy cultures, cream color

later. Drop cultures show spirals, fuseaux and spore clusters characteristic of the gypsum group. This group belongs to the small-spored ectothrix variety, and is believed to be reported for the first time as generally accredited to *Epidermophyton*.

That the species designated "A" and "B" are specifically inclined to attack the nails is indicated by the frequency with which the nail affection follows and coexists with ringworm of the hands and feet among several members of the same family. The possible relation to the group of which *Trichophyton rosaceum* and *T. equinum* are members, or their being new species, is considered, but pending a comparative study with Sabouraud's type cultures definite classification is withheld for a future report in which it is hoped to include a study of additional cases and their etiology.

The frequent coexistence of *tinea cruris* with these nail conditions and the demonstration that in one case the fungus was the same as that in the nails, suggests that species of *Trichophyton* may be responsible for many cases of this affection that is so prevalent and that is generally accredited to *Epidermophyton*.

Some tests of the Sabouraud maltose and glucose are given which show them to be of very much the same composition, both consisting largely of dextrose (glucose). This accords with comparative results of cultures on mediums prepared with these two crude sugars.

That the nail affection will yield to persistent treatment with Whitfield's ointment, combined with thorough scraping of the nails, is demonstrated by a complete cure of two patients in whom all of the nails of one hand were affected.

SUPPLEMENTARY NOTE

More recent investigation since this manuscript was written has pretty definitely established that the species designated *Trichophyton* "A" and probably *Trichophyton* "B" are identical with a species described almost simultaneously in 1910 by Bang¹⁴ as *Trichophyton purpureum* and by Castellani¹⁵ as *Epidermophyton rubrum*. Later Sabouraud,¹⁶ in whose laboratory Bang's work was done, acknowledged the priority of Castellani's discovery and observations.

14. Bang, Henrik.: Sur une trichophytie cutanée a grands cercles causée par un dermatophyte nouveau (*Trichophyton purpureum* Bang), Ann. de dermat. et syph., 1910 (May) p. 225.

15. Castellani, Aldo.: Observations on a New Species of *Epidermophyton* Found in *Tinea cruris*, Brit. J. Dermat. 1910 (May) p. 147.

16. Sabouraud: Trichophytic Eruption Caused by the *Trichophyton rubrum* of Castellani (*Epidermophyton purpureum*, Bang), Brit. J. Dermat., 1911 (December) p. 389.

Bang considered the species to be of American origin. It was noted by both Bang and Castellani as producing a special type of *tinea cruris* with a tendency to spread to other portions of the body.

My findings, especially as to microscopic morphology, agree rather more closely with the descriptions of Bang. I have been unable to find in the literature any previous record of cases of onychomycosis caused by this species, which I believe to be a frequent cause of the nail affection in the southern part of the United States.

OBSERVATIONS ON MEDICAL PHOTOGRAPHY

WITH SPECIAL REFERENCE TO SKIN DISEASES

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NEW YORK

Time is generally lacking for the average physician to become an expert photographer unless he chooses to take up the photographic art as a hobby. I have long been convinced that professional photographers cannot, as a rule, take satisfactory medical photographs. The difficulty lies in posing the subject, as the professional photographer is seldom able to realize exactly what is desired by the physician. This is particularly true in the case of skin diseases. It is for those who desire to make photographic records of their own cases that the following observations, based on personal experience, have been recorded.

Of the various sources of illumination, diffused daylight is in many ways most satisfactory. Direct sunlight, however, is to be avoided except for taking colored photographs (Lumière plates) when the exposure is necessarily long. Daylight photography has its disadvantages, as a properly lighted studio, which is necessary to produce the best results, is seldom at the physician's disposal. It is also slow and requires a great deal of experience, owing to the change of light, properly to judge the time of exposure.

There are several sources of artificial illumination which are used for photography; namely, flashlight (magnesium powder mixture), electric light (studio lamp), and the Cooper Hewitt lamp (mercury vapor). As I have had no personal experience with the Cooper Hewitt lamp, it will not be considered.

Flashlight is perhaps the most desirable form of illumination, if conditions are such that the resulting smoke can be properly removed. If it is desired to take several pictures at one sitting, the ordinary flash bag, which must be emptied after each exposure, is not very convenient. The most feasible method, as suggested to me by Dr. George M. MacKee, is to have a large canvas or metal drum above the flash which collects the rising smoke and leads it outdoors by pipes. A suction pump may be necessary to aid in carrying out the smoke effectively. It is possible at times to connect the pipes with a vent leading to the roof, and not merely to carry the smoke out of the nearest window and allow it to settle as a fine white dust on the windows of an office or apartment beneath. One great advantage of a flashlight is that it can be fairly well standardized by using for each exposure the same

aperture, the same amount of flashpowder, and the same distance of the subject from the camera. As a flash is instantaneous, it is naturally most suitable for restless subjects, such as children, or for parts of the body which are difficult to immobilize, such as the tongue, abdomen,



Fig. 1.—Improper posing of subject; area of body too small, head bent forward, arm outstretched, and background filled with inartistic and distracting objects. Electric light and 7-inch (focal distance) lens were used. Case of psoriasis.

genitals, etc. Another great advantage of flashlight is the intensity of illumination, allowing a very small aperture, which increases the depth of focus.

The so-called studio lamp is a 1,000 watt nitrogen lamp with a blue glass bulb, enclosed in a metal reflector. This is operated on an ordinary 110 volt, direct current. It is a simple and cleanly source of illumination, and one used to best advantage in photographing small

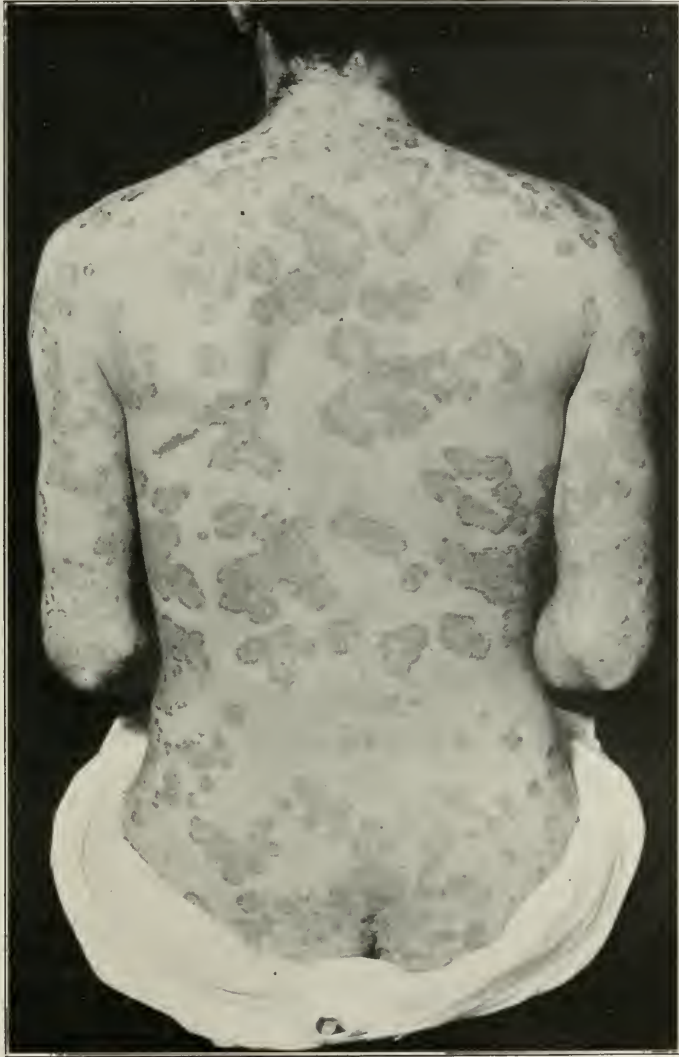


Fig. 2.—Same subject as in Figure 1, properly posed; head erect, shoulders squared, arms falling evenly, clothing neatly arranged. Illumination and lens same as in Figure 1.

areas of the body, such as the head, hands, feet, etc. Like daylight, its action is slow in comparison with flashlight. As the light is rather concentrated, it casts strong shadows, which, however, can be avoided

by using a black background. Unlike daylight, this source of illumination is constant and admits of a certain amount of standardization in making exposures.



Fig. 3.—Proper pose; body erect; probably not so satisfactory or natural as with arms at side. Photograph by daylight: 19-inch lens. Case of psoriasis.

THE SELECTION OF PROPER LENSES

In selecting a lens, it is necessary to consider quality, focal distance, and speed. A good quality of lens, with the necessary corrections for astigmatism and other defects, can now be obtained from a number of

high class manufacturers. To understand better these brief remarks on lenses, explanations are herewith given for those who have not had occasion to study the subject.

The focal distance of a lens is roughly the distance from its center to the ground glass, when an image at infinity (100 feet or more) is sharply focused (on the ground glass). The speed of the lens depends on the ratio of its diameter to the focal distance. To be exact, the speed is proportional to the square of the effective aperture divided by the focal distance. The greater the diameter of the lens, and the shorter its focal distance, the greater will be the resulting speed. Depth



Fig. 4.—Subject lying horizontally on table; suitable position for children or restless individuals; cloth beneath subject too dark; i. e., too much contrast. Gray cloth would have been preferable. Photograph by daylight; 19-inch lens. Case of ichthyosis hystrix.

of focus refers to the range of sharpness forward and back of the object; i. e., the ability of the lens to bring points in different planes sharply into one focus at the photographic surface.

To obtain the finest pictures of portions of the human body, it is necessary to use a lens of long focal distance (from 18 to 20 inches). This, however, lessens the speed, unless the lens has a large diameter, which makes it large and bulky, and greatly increases the cost. There is no doubt, however, that a lens of long focal distance (with the subject necessarily at a long distance from the camera) gives pictures

with the least distortion of perspective. This is shown by the finest photographs taken by my father, Dr. George Henry Fox, with a Dallmeyer lens of 19-inch focal distance. The chief objections, from a practical standpoint, to a lens of long focal distance is that a long gallery is needed, and that unless the lens is very large (and correspondingly expensive) it is rather slow. Probably the ideal lens would be a modern anastigmatic lens of 19-inch focal distance, and rapid action (F 4.5). Such a lens would cost approximately \$450 at the present time. For practical purposes a good rule to follow is to use a



Fig. 5.—Hand against wall, elbow resting on suitable support; fingers look abnormally fat from distortion of perspective, due to too short focal distance of lens. Photograph by electric light; 7-inch lens. Case of ringworm of nails in a negress.

lens whose focal distance is one and one-half times the diagonal of the plate to be covered. Thus, if a 5 by 7-inch plate is used, the focal distance would be about 12 inches.

TECHNIC

One of the essentials for the beginner to learn is the proper posing of the subject. A good rule is to place the subject in a position that will allow as complete muscular relaxation as possible. When pho-

tographing the head, there should be a suitable head rest, which, if possible, should not be allowed to appear in the picture. The best photograph of the back is obtained by having the patient straddle a side chair and grasp the back of the chair with both hands, the head being erect and the shoulders sloping evenly. When photographing a hand it is advisable to rest the entire forearm on some suitable flat surface.

There are many who think that if the lesion in question is properly reproduced the artistic aspect of the picture can be entirely disregarded. Thus many otherwise excellent photographs are injured by careless posing of the patient, or by allowing various extraneous objects to appear in the picture, distracting the attention from the disease or deformity that is being portrayed. Disheveled hair or clothing, head rests, furniture, flower pots or other "scenery" in the background, all offend the eye and lessen the artistic value of the picture. A mistake



Fig. 6.—Proper pose to show extensor surface of forearm and hand; parts at rest, muscles relaxed; cloth under arm too white; i. e., gives too much contrast. A gray cloth would have been preferable. Photograph by daylight; 19-inch lens. Case of rhus dermatitis.

that is frequently made is to have either too much or too little border. The tendency is generally to have too little border, as a result of attempting to make the picture as large as possible. Another practice that is subject to severe criticism is that of photographing too limited an area, with the result that it is difficult or impossible to recognize the anatomic landmarks. In many such pictures it is hard to distinguish between an arm or a thigh unless one of the neighboring joints is included. Photographs of a breast or a buttock may likewise be indistinguishable if the region that is included is too limited.

Next to posing the subject the greatest difficulty is to judge properly the time of exposure. This applies chiefly to daylight photography where weather conditions and time of day, as well as time of year,

must be taken into consideration. In the case of artificial light, this can be more or less standardized. It has generally been my practice to make two exposures when working by daylight or electric light, and a single one when photographing by flash light.

The choice of a camera is not a matter of great importance, though it is preferable to have it mounted on a solid, movable stand instead of on a tripod. The choice of a studio, however, is of great importance for daylight photography, as a properly constructed skylight (preferably with northern exposure) is needed. A black cloth may be used for a background, though I think that the use of black, or of white, causes too much contrast for this purpose. I prefer a wall painted a "battle-



Fig. 7.—Satisfactory pose of foot draped to show sole alone. Photograph by daylight; 19-inch lens. Case of scarlatinal desquamation on sixteenth day (taken at Willard Parker Hospital).

ship gray," or a large piece of canvas. Small pieces of cloth to drape a localized area should also be of a similar neutral color, and the weave of the cloth should be as fine as possible. Reflecting side screens are of value, especially for flashlight work.

Routine developing and printing can fortunately be left to an assistant, or to any good commercial photographer. The best prints for reproduction (halftones) are probably those which are made on glossy printing paper. If this is not obtainable, a good substitute is provided by a glossy developing paper. Blueprint paper for photographic work is unobtainable at present. It can, however, be made

without much trouble by using a mixture of potassium ferricyanid and iron and ammonium citrate (supplied commercially in powder form). While such prints are not suitable for reproduction, they are very convenient for an index of a collection of photographs.

In the choice of photographic plates, speed, color value, and size must be considered. The plates should be reasonably fast, and if



Fig. 8.—Photograph by flashlight; 7-inch lens. Case of hereditary syphilis.

orthochromatic they will give the best color values. I feel that it is best to adopt a standard-sized plate and one that is not too large. Like my father, I have used 5 by 7-inch plates for many years. A larger plate than this is unnecessarily expensive, and harder to handle and file. When the photographic collection becomes large, it is convenient to file the negatives in boxes, placing them in alphabetical order, on end, as in the vertical filing system of papers.

My experience in color photography (Lumière plates), which naturally appeals to the dermatologist, is limited. The plates require a long exposure, are expensive and, what is of greatest importance, cannot be reproduced on paper.

CONCLUSIONS

1. Satisfactory medical photographs cannot be made by the average professional photographer, as he is ignorant of the exact anatomic condition which is desired to be reproduced.

2. To obtain a collection of good medical photographs it is generally necessary for the medical man to learn at least to pose the patient, and to make the exposure himself.

3. Developing and printing can be satisfactorily done by professional photographers.

4. Daylight, flashlight and electric light (studio lamp) are all suitable sources of illumination, though each has certain advantages and disadvantages.

5. It is urged that care be taken to make artistic as well as anatomically accurate photographs.

6. The lens should be of good quality and of reasonably long focal distance, if the length of the gallery permits.

7. A standard size should be adopted for photographic plates, 5 by 7 inches having been found very satisfactory and convenient.

616 Madison Avenue.

VISCERAL SYPHILIS

SYPHILIS OF THE LUNG *

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Acquired pulmonary syphilis is exceedingly rare pathologically, and it is even more rare as a clinical picture. In congenital syphilis, it is a not infrequent pathologic picture in the form of the well known white pneumonia. As a diffuse sclerosis and as small gummas, it is also encountered clinically, and subsequently it is encountered as a pathologic picture in the congenital form of the disease.

As in syphilis of the gastro-intestinal system, in which the symptomatology is so like that of other gastro-intestinal disease, so also in lung syphilis we are dealing with a condition in which clinically there is absolutely no diagnostic picture. In its various forms, syphilis of the lung may present itself with a clinical picture of any phase of pulmonary disease. For this reason, the condition probably exists to a greater extent than is indicated by either the clinical or the pathologic reports.

OBSERVATIONS TO THE PRESENT TIME

Reference to pulmonary disease, associated with syphilis and, at least as indicated, possibly due to the latter, is found as early as the sixteenth century in the works of Paracelsus,¹ Pincto,² von Grafenberg,³ Coesalpinus,⁴ and Paré.⁵ More accurate observations and those more worthy of attention are found in the eighteenth and the early

* Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Udo J. Wile, M.D.

1. Paracelsus: *Opera Medica*.

2. Pincto, quoted by Fournier: *Traité de la Syphilis* 2:712.

3. Von Grafenberg, Schenk: *Jour. Observationen medicarum, rararum, navarum, admirabilium et monstrarum*, 1596.

4. Coesalpinus, Andreas: *Praxis universae artis medicae*, 1606.

5. Paré, Ambroise: *Oeuvres completes* 2:526.

nineteenth centuries, in the writings of Boerhave,⁶ Astruc,⁷ Laennec,⁸ and Morgagni.⁹

The first clear cut anatomic description of pulmonary syphilis is found in the writing of Depaul¹⁰ in 1850. Virchow's¹¹ clinical description is found eight years later, in 1858. The latter's description of white pneumonia still stands as a classic monograph on the subject.

The attention drawn to the possible connection between pulmonary disease and syphilis as indicated in the aforementioned writings gave rise to an enormous number of reports of cases of "pulmonary syphilis."

This large group of cases just antedates Koch's monumental work on tuberculosis in 1875; and it seems probable that the cases reported for the most part were those in which syphilis occurred coincident with pulmonary tuberculosis, or that many were actually cases of frank tuberculosis thought to be syphilis. Coincident with the acceptance of pulmonary phthisis as tuberculosis, it is a striking fact that cases of pulmonary syphilis ceased to appear in the literature.

The infrequency of the condition is indicated by the fact that, in 1882, Carlier¹² was able to collect but twenty cases of undoubted lung syphilis studied at necropsy. The following two years yielded but eight more cases, collected by Hiller.¹³ Notwithstanding this apparent rarity, an occasional writer would still speak of the condition as frequent. Thus Pancritius¹⁴ thought that it was a common condition and responsible for the death of many people each year.

In 2,500 necropsies in Johns Hopkins Hospital, however, Osler¹⁵ found twelve cases, which appears to be a fairly large number. Downing,¹⁶ however, found no cases in 3,000 postmortems performed at the Massachusetts General Hospital. Massia¹⁷ describes two cases in 6,000 necropsies in Copenhagen. The various differences of percentages in these figures can undoubtedly be explained by the difference of opinion as to the criteria of syphilitic involvement.

Writing from Warthin's laboratory in 1920, Carrera¹⁸ describes changes in the lung in twelve cases out of 152 necropsies in known

6. Boerhave, Hermann: *Tractatio medica practica*.

7. Astruc: *De Morbus Venereis*, Paris, 1736, p. 318.

8. Laennec, R. T. H.: *Treatise on the Diseases of the Chest and on Mediate Auscultation*, 1834.

9. Morgagni: *De Sedibus et Causis Morbarum Venetio*, 1761, p. 227.

10. Depaul: *Gaz. méd. de Paris*, 1851; *Bull. de l'Acad. de méd.* **17**:503.

11. Virchow: *Arch. f. Path. Anat. u. Physiol.* **15**:310, 1858.

12. Carlier, Georges: *Thèse de Paris*, 1882.

13. Hiller, A.: *Ueber Lungensyphilis und Syphilitische Pthisis*, *Charité-Ann.* **9**:182-282, 1884.

14. Pancritius, F. W. T.: *Ueber Lungensyphilis*, Berlin, 1881.

15. Osler, William: *System of Medicine* **2**:170.

16. Downing: *Boston M. & S. J.* **172**:898, 1915.

17. Massia: *Le poumon syphilitique*, *Gaz. d. hôp.* **84**:1829, 1917.

18. Carrera: *Am. J. Syphilis* **4**:1, 1920.

syphilitic cases. Postmortem findings indicating syphilitic pulmonary disease have been recorded during the last decade or two in the writings of these men: Kuhn,¹⁹ Brandenburg,²⁰ Schmorl,²¹ Sugai,²² Robertson,²³ Shingu,²⁴ Favre and Savy,²⁵ Clayton,²⁶ Lindvall and Tillgren,²⁷ Milne,²⁸ Tanaka,²⁹ Kielty,³⁰ Carrera¹⁸ and Patino.³¹

DIFFICULTY OF RECOGNITION

Difficult as is the gross pathologic picture, the clinical picture of pulmonary syphilis is even more difficult of recognition. In the last analysis, it must be admitted that with the present standards, no case of clinical pulmonary syphilis can be absolutely accepted without a pathologic examination.

It is now a well accepted fact that syphilis and tuberculosis may, and frequently do, occur together. It has been a frequent observation by us that latent tuberculosis is very apt to become activated in the presence of active syphilis. The net result of both processes pathologically, fibrosis and cavitation in the lung, gives rise to a set of parallel symptoms indistinguishable not only in local signs but also in general body reaction.

Conversely, it may be accepted that a pure syphilitic process in the lung, existing unrecognized, constitutes an admirable site for the implantation of the tubercle bacillus.

While the proof of clinical pulmonary syphilis must be sought and found at the postmortem table, there is, nevertheless, a small group of cases in which the evidence is even more than presumptive that one is dealing with pure syphilis of the lung. These are cases in which, for the most part, the processes are atypical, both clinically and in their course. There are cases in which the pulmonary symptoms may be

19. Kuhn, *Charité-Ann.* **19**:438, 1905.

20. Brandenburg: *Ein Beitrag zur Lungensyphilis*, *Beitr. z. Klin. d. Tuberk.* **10**:183, 1908.

21. Schmorl: *Verhandl. der deutsch. path. Gesellsch.* **11**:281, 1907.

22. Sugai: *Centralbl. f. allg. Path. u. path. Anat.* **20**:193, 1909.

23. Robertson: *J. Path. & Bacteriol.* **15**:45, 1911.

24. Shingu: *Wien. klin. Wchnschr.* **23**:970, 1913.

25. Favre and Savy: *Pseudo-epithelioma syphilitique de l'adulte*, *Arch. de méd. expér. et d'anat. path.* **25**:363, 1913.

26. Clayton: *Am. J. M. Sc.* **129**:563, 1905.

27. Lindvall and Tillgren: *Beitr. z. Klin. d. Tuberk.* **24**:311, 1911.

28. Milne: *Lung Syphilis*, *Am. J. M. Sc.* **142**:408, 1911.

29. Tanaka: *Arch. f. path. Anat.* **108**:429, 1912.

30. Kielty: *Syphilis and Tuberculosis in the Same Lung*, *New York M. J.* **104**:252, 1916.

31. Patino: "Sifilis Pulmonar." Buenos Aires, Spinelli, 1916.

either coincident with early syphilis or present with manifest constitutional syphilis of other viscera, in which prompt amelioration or even complete disappearance of signs and symptoms results on the institution of antisyphilitic treatment. Such cases as these, if carefully worked up, in which tuberculosis has been eliminated in all probability, and in which the last proof is lacking by reason of the patient's survival, must be accepted as presumptive examples of syphilitic pulmonary disease. During the last two decades reports of about fifty such cases have been found in the literature. For the most part they have been carefully studied by competent observers, and we feel that they may justifiably be taken as various examples of syphilitic disease, as far as clinical medicine can go in the diagnosis of this condition. Such cases are reported by these men: Stengel,³² Hughes and Wilson,³³ Kayser,³⁴ Pelton,³⁵ Forsythe,³⁶ Roussel,³⁷ Burnham,³⁸ Binder,³⁹ Culver,⁴⁰ Easton,⁴¹ Landis and Lewis,⁴² Bauch,⁴³ Perret,⁴⁴ Castex and Denis,⁴⁵ Morris,⁴⁶ Watkins,⁴⁷ Wood,⁴⁸ Dexter,⁴⁹ Phipps,⁵⁰ Witherspoon,⁵¹ Hall,⁵² Klotz,⁵³

32. Stengel, A.: Syphilis of the Lungs Simulating Pulmonary Tuberculosis, Univ. Penn. M. Bull. **16**:89, 1903.

33. Hughes and Wilson: Med. News **86**:351, 1905.

34. Kayser, K.: Fortschr. a. d. Geb. d. Roentgenstrahlen **22**:214, 1905.

35. Pelton: Med. Rec. **77**:146, 1910.

36. Forsythe: Gumma of the Lung, Proc. Roy. Soc. Med., Lond. 1911-1912, p. 186.

37. Roussel: New York M. J. **98**:600, 1913.

38. Burnham: Syphilis of the Lung, Boston M. & S. J. **151**:411, 1914.

39. Binder: Syphilis of the Lung Simulating Pulmonary Tuberculosis, Med. Rec. **86**:330, 1914.

40. Culver: An Instance of Pulmonary Syphilis Closely Simulating Tuberculosis, J. A. M. A. **64**:335 (Jan. 23) 1915.

41. Easton: Syphilis of the Lung, Med. Rec. **88**:652, 1915.

42. Landis and Lewis: Latent Syphilitic Infections of the Lung, Am. J. M. Sc. **150**:195, 1915.

43. Bauch: Report of Two Cases of Syphilis of the Lung, Med. Rec. **89**:906, 1916.

44. Perret: Report of a Probable Case of Lung Syphilis, New Orleans M. & S. J. **69**:191, 1916-1917.

45. Castex and Denis: Rev. Assoc. méd. argent. **26**:303 (April) 1917.

46. Morris, F. M. F., Jr.: Syphilis of the Lung, Am. J. Syphilis **2**:231, 1918.

47. Watkins: Roentgen Diagnosis of Lung Syphilis, Am. J. Syphilis **1**:760, 1917.

48. Wood: Syphilis of the Lungs, Boston M. & S. J. **175**:677, 1916.

49. Dexter: Pulmonary Syphilis, Cleveland M. J. **16**:147, 1917.

50. Phipps: Pulmonary Syphilis, Boston M. & S. J. **176**:390, 1917.

51. Witherspoon: Syphilis of the Lungs, South. M. J. **11**:275, 1918.

52. Hall: Gumma of the Entire Left Lung, Lancet **145**:779, 1918.

53. Glotz: Differentiation of Syphilitic and Tubercular Pulmonary Lesions, Calif. State J. M. **16**:82 (Feb.) 1918.

Post,⁵⁴ Boudet,⁵⁵ Bensaude and Emery,⁵⁶ Boisliniere,⁵⁷ Zehner⁵⁸ and Patino.³¹ From a study of these cases, and of a few which belong in this group which we have been able to study in the university hospital, it appears that clinical pulmonary syphilis in the acquired form of the disease may occur: (1) as isolated gummas of the lung; (2) as diffuse syphilitic fibrosis, and (3) possibly as a diffuse bronchopneumonia.

THREE FORMS OF VISCERAL SYPHILIS

The reaction of syphilis in the pleura has already been discussed in another place. In a general way it may be stated here that syphilitic pleuritis may occur independently of pulmonary involvement in the form of a dry pleurisy similar to that occurring in tuberculosis, but that effusion, together with pleuritic pain, is an occasional happening in syphilis. Where the lung is extensively involved, secondary pleuritis, as in tuberculosis, is almost inevitable. The possible exception to this is in those cases in which a massive syphilitic infiltrate is found at the hilum of the lung, or where the process does not reach the pleuritic border.

Of the above mentioned three forms, chronic fibroid changes in the lung are described as the most frequent. Undoubtedly, some of these at least are the result of the breaking down and slow absorption of larger and smaller gummas, and it is not unlikely that, as in syphilis of the liver, one is dealing not so much with a variety of form as with a difference in the time at which the patients are studied. Thus, for example, it may be accepted that the interstitial fibroid condition, the so-called syphilitic phthisis, is a late result, being, in fact, an analogous picture to the interstitial hepatitis found as a terminal picture either of isolated or of diffuse syphilomas in the liver.

The picture of "syphilitic bronchopneumonia" constitutes a disputed field. That symptoms of an acute or subacute pneumonia with diffuse patches of consolidation, either more or less severe, are occasionally met in the course of pulmonary syphilitic disease is accepted. The explanation that these symptoms are themselves due to syphilis, however, is disputed. Councilman,⁵⁹ Gambrini,⁶⁰ Birch-Hirschfeld,⁶¹

54. Post: Two Cases of Syphilis of the Lungs, *Boston M. & S. J.* **174**: 876, 1916.

55. Boudet: *Trois Observations de Syphilis de Poumon*, *Paris méd.* **23**: 493, 1917.

56. Bensaude and Emery: *Bull. et mém. Soc. méd. d. hôp. de Par.* **1**:137, 1913.

57. Boisliniere: Reaction of the Lung to Syphilis, *Am. J. Syphilis* **4**:466 (July) 1920.

58. Zehner: *Schweiz. med. Wchnschr.* **50**:651 (July 22) 1920.

59. Councilman: Syphilis of the Lung, *Bull. Johns Hopkins Hosp.* **11**: 34, 1891.

60. Gambrini, quoted in *Brit. M. J.* **1**:21, 1881.

61. Birch-Hirschfeld, F. V.: *Lehrbuch der speziellen Pathologie*, Leipzig **2**:186, 1899.

Orth,⁶² Kaufman,⁶³ Adami,⁶⁴ and others believe that this chain of symptoms is not due to syphilis itself, but that it is due to a secondary pneumonic process superimposed on a lung weakened by syphilis.

Against this view is that held by Neumann,⁶⁵ Fowler and Godlee,⁶⁶ Fournier,⁶⁷ Dieulafoy,⁶⁸ Aufrecht,⁶⁹ and others, who believe that the condition is a true syphilitic pneumonia.

Having ourselves seen such symptoms occurring coincident with the softening of a large syphilitic infiltrate in the lung, such softening associated with definite signs of consolidation, fever and dyspnea, we are inclined to subscribe to the view that resolving or activating changes in the lung due to syphilis may simulate very closely the picture of bronchopneumonia.

Such symptoms as those just outlined may occur from time to time in an unrecognized case of syphilis in which it is thought that the patient is suffering from pulmonary phthisis. Examples of this are found in the cases reported by Witherspoon⁵¹ and Dexter.⁴⁹ Dieulafoy⁶⁸ has described one case in which the picture was that of a rapidly progressive tuberculosis. A case, observed by us, similar to this in some of its features may be found in the report given herewith.

Gumma of the lung, recognizable as such clinically and pathologically, is said to be exceedingly rare. Its existence has been doubted by Cornil⁷⁰ and others. We believe, however, that it is not so infrequent as the initial stage of a fibrosis and of later cavitation. When found, the gumma is somewhat more frequently described as occurring in the right lung, usually in the middle or lower lobe, and frequently near the hilum. Subpleural gummosis involvement, however, is described as more common in their experience by Brandenburg²⁰ and by Rolleston.⁷¹ The clinical picture of gummatous pulmonitis depends entirely on the location of the process and the stage of its development. Seen in the hilum of the lung, it may present itself as an accidental finding with but few symptoms, or on the other hand, as one of us has seen it, it may present itself with enormous pressure symptoms suggesting those of a mediastinitis due to malignant disease. Seen

62. Orth: *Lehrbuch der speziellen Pathologie und Anatomie*, Berlin, **1**: 480, 1887.

63. Kaufman: *Lehrbuch der speziellen Pathologie*, Ed. 5, 1909, p. 295.

64. Adami: *Textbook of Pathology*, Ed. 2, Philadelphia, Lea & Febiger, p. 555, 1914.

65. Neumann: *Spec. Path. u. Therap.*, Nothnagel **33**:563, 1891.

66. Fowler and Godlee: "Diseases of the Lungs," p. 429.

67. Fournier: *Traite de la Syphilis* **2**:710.

68. Dieulafoy: *Textbook of Medicine*, Collin's translation, **1**:231, 1914.

69. Aufrecht, E.: *Die Lungenentzündungen*, *Spec. Path. u. Therap.*, Nothnagel **14**:284, 1899.

70. Cornil and Martineau: *Soc. Anat.* 1862, p. 486.

71. Rolleston: *Tr. Path. Soc.*, London **42**:50, 1891.

either in the hilum, or in the subpleural portion of the lung, when the process is older and breaking down, and softening has begun, the clinical picture may be that of an ulcerative phthisis, or bronchiectasis, or of slowly resolving pneumonia.

In a case under our own observation in which a gumma was found to have developed in a case of heredosyphilis, we were able to study the process almost from its inception to the end-stage of extensive cavitation. In this case the process was indistinguishable except in point of its location from that of chronic ulcerative phthisis, with the end-result of cavity formation.

Other cases of probable gumma of the lung are described by Delepine and Sisley,⁷² Fowler and Godlee,⁶⁶ Osler,¹⁵ Patino,³¹ Brandenburg,²⁰ Rolleston,⁷¹ Rossle,⁷³ Tanaka,²⁹ and others.

Chronic interstitial pneumonitis due to syphilis is the most common form of accepted syphilitic pulmonopathy. Pathologically, this is the expression and end-result of all other syphilitic processes. This stage, as it may properly be called, of syphilitic lung disease is that most frequently studied clinically. It is in this form that symptoms are most frequently encountered, due either to a loss of lesser or greater portions of pulmonary tissue, or to their loss of function. The chief characteristics of the condition pathologically are a radiating fibrosis extending out from the hilum through the bronchi, and of bands extending from the pleura into the substance of the lung. Associated with this are isolated fibroid masses throughout the substance of the lung representing areas of more diffuse syphilomatous tissue.

The extensive fibrosis results in a marked diminution in the air content of the lung; the fibrosis in and about the bronchi gives rise to symptoms of dyspnea, to coughing, and to vascular changes characteristic in the lung of syphilis, as elsewhere, leading to occasional hemoptysis. That extensive syphilitic phthisis, so-called, can exist without symptoms is evidenced by the interesting case reports of Milne. Two patients presented no symptoms referable to pulmonary disease during life, but extensive syphilitic fibrosis of both lower lobes was determined at necropsy. In cases in which symptoms are prominent, these are of so variable a character, and are so variable in their degree, that it may be stated that there is nothing characteristic in the clinical picture which would differentiate them from the mild or grave symptoms of clinical fibroid phthisis.

In the presence of such symptoms, with a total absence during many examinations of the demonstration of tubercle bacilli, and particularly when such a clinical picture is associated with syphilis in other viscera, it may be presumed that the picture is due to syphilis. It

72. Delepine and Sisley: *Tr. Path. Soc.*, London, **411**:141, 1891.

73. Rossle: *München. med. Wehnschr.* **65**:1199, 1918.

must be added here, however, that the demonstration of tubercle bacilli in the sputum of a suspected case in no way diminishes the possibility of syphilitic disease, when it is remembered that the two are frequently associated.

PROGNOSIS

In a general way the prognosis of pulmonary syphilis may be said to vary directly with the time at which a correct diagnosis is established. In the early cases, in gummas and in the earlier stages of the chronic fibroid type, the prompt institution of antisyphilitic treatment undoubtedly offers a fair prognosis in the condition. If extensive fibrosis and destruction have taken place, a condition analogous to that seen in chronic interstitial hepatitis is found. A marked general betterment in the patient's condition may be expected as a result of the institution of treatment directed to the disease as a whole, but little change can be expected in the signs or symptoms of the pulmonary condition. The prognosis is materially influenced, however, by the association of tuberculosis. The presence of both conditions adds a more serious prognosis than either one or the other case alone.

The cases of presumptive syphilitic pulmonitis herewith reported have been seen and studied by us at the university hospital, and in the private practice of one of us:

REPORT OF CASES

CASE 1.—Chronic interstitial syphilitic pulmonitis.—*History.*—A man, aged 37, entered the university hospital, Nov. 5, 1920, having been referred from the department of internal medicine for *tabes dorsalis*. His complaint was weakness and difficulty in walking. The family history had no bearing on his present illness. There was no family history of tuberculosis or other lung trouble. The patient had had a primary syphilitic sore eighteen years before, which he says was not followed by any secondary manifestations. He had not received any treatment for the condition. He had been married for eight years and had three living children. His wife had had one miscarriage three months ago at the end of the second month of pregnancy. One year previous to admission he had noticed that if he walked in the dark he staggered and had great difficulty in keeping his balance. This condition had been getting gradually worse during the last year. He had had occasional sharp shooting pains in the legs, also dating back one year. Ten days previous to admission, he developed a cough and expectoration, some of which had been tinged with blood. There was no history of a definite hemophthisis. The patient had not lost weight noticeably, had not been short of breath, nor had he had night sweats.

Examination.—He was poorly nourished and emaciated. He showed many of the classical signs of *tabes dorsalis*, having Argyll Robertson pupils, marked swaying in the Rhomberg position, absent knee and Achilles reflexes, and a typical ataxic gait. The chest, which particularly interests us, presented considerable retraction of the interspaces. On respiratory excursion, there was a slight lagging of the right side. On percussion, there was marked dulness over the right apex and base in the back. The percussion note throughout the remaining part of the lungs was normal. On auscultation, the breath sounds,

spoken and whispered voice, were exaggerated over the right apex and upper lobe. The breath sounds, spoken and whispered voice, were of normal intensity throughout the remaining part of the lungs. There were a few scattered crackling and bubbling râles at both apices, which were more marked in the right.

Roentgen-Ray Examination: Dr. Porter reported these findings:

"The left lung shows nothing unusual. On the right side the apex is obscured by a rather thick, smoky shadow. From the third to the sixth rib,



Fig 1 (Case 2).—Extensive fibrosis of both lungs, most marked about the hilum and in the lower lobes, together with a small isolated cavity in the left lower lobe; the cavity is indicated by the arrow.

inclusive, there is a very heavy shadow of thickened pleura in which there are definite localized areas of pronounced fibrosis. From the fifth to the eighth rib posteriorly the lung is comparatively free. Below this there is a curious elevation superimposed upon the outline of the diaphragm with a conical shape which probably represents a consolidation. The lateral view shows this mass to lie anteriorly in the pleural angle. Its anterior end is of a high degree of density

and cannot be distinguished from the upper surface of the diaphragm. Posteriorly and superiorly, it gradually fades into the surrounding lung substance and there appears to be a space of at least 1 inch between it and the anterior surface of the nearest vertebra behind."

A subsequent roentgen-ray reading was made by Dr. Van Zwaluwenberg:

"The density in the right side of the chest is unusually uniform, and free from the irregularities in density and cavity formation and the dense localized sclerosis of tuberculosis. The impression is rather that of a diffuse interstitial thickening, with a wedge-shaped distribution. There is undoubtedly considerable cicatricial tissue in the pleura, as is shown by its thickening and by the reduction of the width of the interspaces. The pleura is also involved over the extreme apex. The mass in the lower lung is an exceedingly unusual picture in tuberculosis. It has a density almost uniform, not so great as that of the liver and not sharply circumscribed, but with a rather fringed border. There is comparatively little retraction of the mediastinum toward that side. The distinction between tuberculosis and syphilis cannot be sharply drawn on these findings. While the first impression is that of tuberculosis, syphilis might easily produce the same type of lesion and might so modify tuberculosis as to produce the unusual picture of this plate. The total absence of any suggestive sign in the left lung is also puzzling, since it is scarcely conceivable that so extensive a tuberculosis could occur without bilateral involvement."

Treatment and Results.—Repeated examinations of this patient's sputum during his stay in the hospital were negative for tubercle bacilli. He received during his stay in the hospital five intravenous and four intraspinal injections. During this time he gained weight and showed continuous improvement. In addition to the increase in weight, his cough diminished, and his general health was better than it had been for months past. A letter written to the patient four months after his discharge elicited the response from him that he is able to do light work, that he feels exceptionally well and is in every way improved.

Résumé.—In a patient with a well developed tabes there occurs the fairly acute onset of pulmonary disease associated with a rather massive infiltrate occupying the lower portion of the left lung. The afebrile nature of the condition, the extensive process and the absence of general reaction, the total absence of tubercle bacilli in repeated examinations of an abundant sputum, and the prompt amelioration under antisyphilitic treatment, make this case a presumptive one of pulmonary syphilis.

CASE 2.—*Chronic interstitial pulmonitis with cavitation, in hereditary syphilis.*—*History.*—A boy, aged 15, first entered the university hospital in May, 1914, with multiple arthritis involving practically all the larger joints, with no symptoms referable to lung disease. He showed a large number of stigmas of hereditary syphilis, namely, prominent bosses, both parietal and frontal, wide nasal bridge, Hutchinson's teeth, scaphoid scapulae, ulnar deviation of the fingers, saber shins and rhagades at the angles of the mouth. After one week of sodium salicylate therapy with practically no change in the joints, the patient was put on artisyphilitic therapy. He improved rather rapidly, so that in a few weeks he could walk very well and left the hospital.

In October, 1915, he again came to the hospital, partly because of the recurrence of arthritis in his knees and ankles, and partly because of symptoms of lung disease. After leaving the hospital in June, 1914, the patient states that he felt fine until March, 1915, when he had an attack of "pleurisy." He developed a cough and raised some sputum. He never had had a hemorrhage from the lungs. His cough had continued since March, and he had lost a number of

pounds in weight. He spent a short time in a tuberculosis sanatorium but, after frequent negative sputum examinations, the physician discharged him, and sent him here for antisymphilitic treatment, believing the condition to be syphilitic.

Examination.—Dr. Hewlett's examination of the chest at this time revealed the following: Slight tendency to roundness existed over the lower portion, with prominence of both clavicles. Movements behind were equal and coarse, rhonchi could be felt over both bases. Tactile fremitus well felt everywhere. The backs were resonant, with possibly a slight impairment of the right interscapular region. The lower border of the left lung was fixed, but at the normal level. Also some impairment was noted over the left base and numerous crackling râles were heard at both bases, more particularly at the left. In the left interscapular region a decided increase of whisper was noted, and below the angle of the left scapula an almost bronchial whisper was heard. The front right upper lung moved better than the left. Tactile fremitus was increased on the right. The lungs were hyperresonant. Roentgenograms were taken and confirmed by Dr. Hewlett's findings. The plates showed extensive fibrous involvement of both lungs, most marked about the hilum and in the lower lobes, with mottling of the mesial portion of the left apex. A dense band of scar tissue was present in the interlobular septum between the right upper and middle portions. There was marked local exaggeration of the bronchial tree in various places. A small isolated cavity in the left lower lobe, about three fourths of an inch radially inward from the seventh rib in the post-axillary line, was noted.

Treatment and Results.—During his second stay, this patient remained in the hospital under observation for three months. During this time he received vigorous antisymphilitic treatment, directed largely to the arthritis and to the keratitis, both of which cleared up. During this time he gained about 20 pounds in weight, was markedly benefited in every respect, and all of the symptoms referable to the lungs cleared up very promptly.

Résumé.—In a patient with well marked stigmas of hereditary syphilis there occurred the acute onset of pulmonary symptoms, suggestive of tuberculosis. These clinical findings were associated with very extensive fibroid changes of both lungs, particularly marked about the hilum and in the lower lobes, with the production of a small isolated cavity in the left lower lobe. Repeated examination of an abundant sputum was entirely negative for tuberculosis, and there was a relatively afebrile course during the entire period of his stay. These findings are more than suggestive of a presumptive case of chronic fibroid syphilitic pulmonitis with cavitation.

CASE 3 (A private case of Dr. Wile).—History.—The patient presented herself on account of an extensive eruption over the body which was thought by her to be tuberculosis. She believed this as she had previously spent considerable time in the university hospital for what was diagnosed as pulmonary tuberculosis. The onset of the "tuberculosis" dated from an injury to the chest wall sustained in a railroad accident.

Examination.—There was an extensive nodulo-ulcerative syphilid of the entire body. The onset of the supposed tuberculosis antedated the cutaneous eruption by four years. During all of this period she had been having active signs of pulmonary disease in the form of weakness, sweats, abundant sputum, an afternoon temperature, shortness of breath, and progressive loss of weight. Dr. Hewlett, who examined the patient at the time of her first stay in the

university hospital, reported that she was a fairly well nourished woman, aged 35, weight, 128 pounds, height, 5 feet, 4 inches, temperature, 98, pulse, 84, and respirations, 18.

Thorax: This was fairly broad and short. The epigastric angle was greater than the right angle. There was fairly good resonance in each apex. Percussion note was elicited on both sides. There was harsh vesicular breathing in both apexes with prolonged expiration, more marked on the right. Loud bronchovesicular breathing was noted over the right upper lobe, with lack of tactile fremitus over this area. The whispered and spoken voice was louder in the upper right lobe. The remainder of the examination was negative. Daily examination of the sputum over two weeks was uniformly negative for tubercle bacilli.

When seen later by one of us for the cutaneous syphilis, the patient had not materially changed in appearance. Examination of the lungs made at this time revealed a very diffuse process over both lungs, more particularly marked near the bases. There was impairment of the percussion note over both sides of the back, but not any definite areas of discrete dullness. The clinical picture at this time was in no way different from that of a chronic fibroid tuberculosis.

Treatment and Results.—On the institution of antisyphilitic treatment the patient's eruption vanished almost immediately; her coughing ceased at once; she experienced relief from all of her symptoms, and her weight increased considerably. After three months' observation she stated that she was as well as she ever had been. She was discharged at this time with instructions to her referring physician to continue her treatment in the form of mercurial inunctions and potassium iodid. The patient remained in good health until 1918, when, during the epidemic, she contracted influenza. She lingered with an apparently residual unresolved pneumonia and died in August, 1919.

Résumé.—In a woman, aged 35, there occurred the onset of acute pulmonary symptoms following an accident. The symptoms were of a diffuse process in both lungs, localized at the bases. Prolonged observation in the university hospital resulted in a diagnosis of chronic ulcerative phthisis, notwithstanding the repeated negative examination of the sputum for the tubercle bacilli. Three years after her discharge from the hospital, she was seen and treated for a diffuse nodular syphilid of the body. During this time there had been no marked change in her general condition. The institution of antisyphilitic treatment resulted in a complete clinical cure of both the syphilid and the pulmonary symptoms.⁷⁴

74. In addition to the references already given, the following will be found of interest:

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A CASE OF PROBABLE PARAFFIN-OIL TUMOR

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In March, 1920, Mook and Wander¹ described for American literature, on the basis of a considerable series of cases, a foreign-body tumor of the arm, essentially a modification of the familiar "paraffinoma," following the hypodermic administration of adulterated camphorated oil in which the olive oil of the pharmacopeial preparation was replaced by liquid petrolatum. The preparation apparently had been used in the treatment of influenzal pneumonia. Clinically the paraffin-oil tumor described by Mook and Wander consists of a brawny indurated and nodular infiltration of the arm having the histologic structure of a granuloma in the inflammatory phase and of a paraffinoma in the quiescent or fibrous stage.

CASE REPORT

Clinical Appearance of Tumor.—The clinical appearance of the tumor in the case reported was typical of the inflammatory phase. Chains and nodules extended from the lesion in the larger part of the anterior and posterior surfaces of the left upper arm into the axilla and from the lower margin of the lesion downward toward the elbow. This feature of the clinical picture, as Mook and Wander have pointed out, is especially likely to suggest tuberculosis or malignant neoplasia. Our clinical diagnosis of paraffinoma was subsequently confirmed by Drs. Wile, Foerster, and Irvine, who saw the patient while visiting the clinic. Mook and Wander have pointed out that tuberculosis is the usual diagnosis made by the general pathologist in these cases because the granulomatous architecture, with whorls of epithelioid cells and Langhans' giant cells, inevitably suggests such a diagnosis to one who has not seen the clinical picture.

Microscopic Examination.—In our case a large piece of tissue was excised for diagnosis. In the tissue excised in this case were innumerable "tubercles" consisting of dense whorls of epithelioid cells with giant cells in and between the whorls (Figs. 1 and 2). The Swiss-cheese structure is much less conspicuous than in the paraffinoma, owing to the greater fluidity of the oil and the consequent wide distribution of the foreign substance. Necrosis may occur in such tumors, but was not conspicuous in our case. Broders believes that there was evidence of caseation, although we were unable to identify it in the

1. Mook, W. H., and Wander, W. G.: VII. Camphor Oil Tumors, Arch. Dermat. & Syph. 1:304-318 (March) 1920.

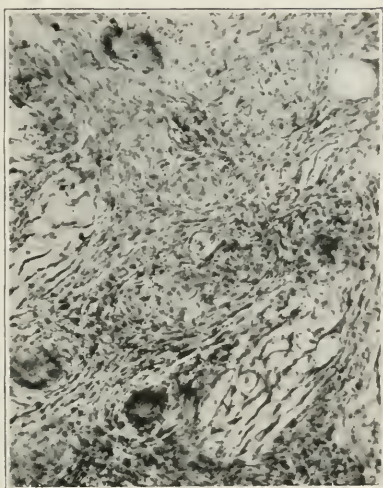
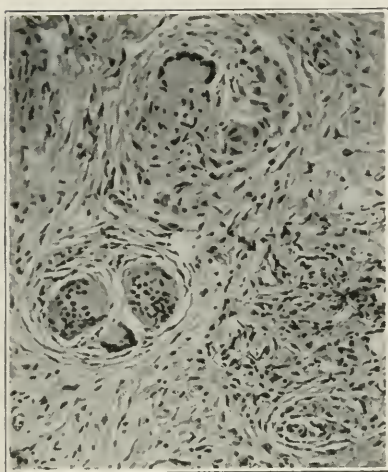


Fig. 1.—Pseudotubercles with giant cells; paraffin section.

Fig. 2.—Granulomatous structure of tissue; oil vacuoles, and pseudotubercles.

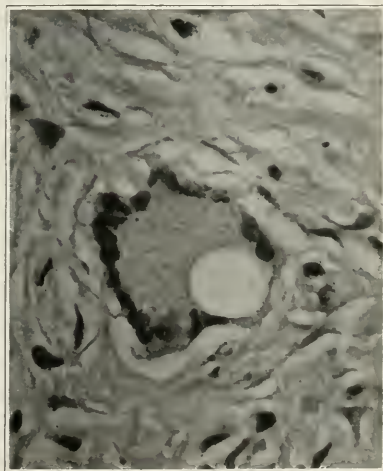
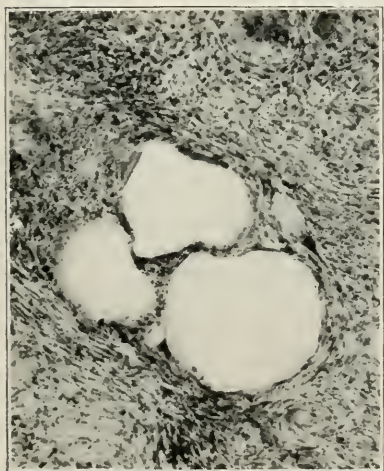


Fig. 3.—“Swiss cheese” appearance due to encapsulated paraffin oil. Frozen section stained with sudan III (oil staining light yellow) showing a film of oil still adherent to the sides of the vacuoles.

Fig. 4.—Giant cell enclosing oil vacuole.

portion studied by us. It is worth while to recall that Cornet and Kossel² and Lewandowsky³ have pointed out that the formation of tubercles without caseation may be interpreted as a foreign-body reaction to the tubercle bacillus. The high lipid content of the organism may be compared to the paraffin oil in its power to produce a tuberculoid reaction of the type seen in this case. Vacuolation with beginning fibrous encapsulation of the oil was apparent. The efforts of the proponents of paraffinoma were centered on a demonstration of the presence of the oil in the vacuoles. This was accomplished by one of us (Scholl), who in cooperation with Dr. Robertson prepared sudan III preparations, in which the foreign oil could be distinguished from the human fat by the fact that it stains a light yellow rather than the deep orange of true fat. In a photomicrograph of such a preparation the thin layer of paraffin oil could be demonstrated still adherent to the wall of the vacuole (Fig. 3). A number of the giant cells contain what are apparently large oil vacuoles (Figs. 4 and 5).

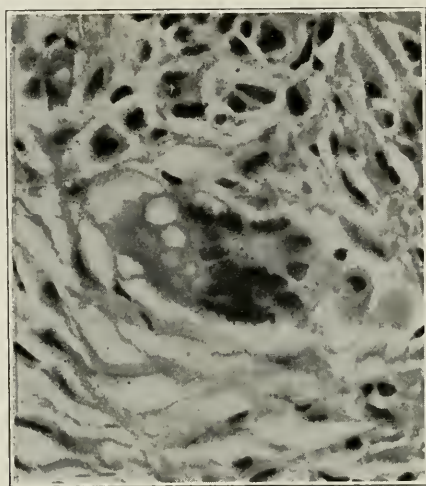


Fig. 5.—Giant cell and oil vacuoles.

Animal inoculations of paraffin oil have been made, but considerable time must elapse before a decisive result can be expected. The proponents of the diagnosis of tuberculosis thoroughly searched the excised tissue for tubercle bacilli and made two guinea-pig inoculations, both of which have been negative. No acid-fast bacilli have been demonstrable in the tissue examined.

History.—The deceptive history and peculiar sequence of events in this case deserve special mention. The patient does not recall having received anything hypodermically except typhoid vaccine in the arm. Eighteen months before, however, he had had influenzal pneumonia and was unconscious from morning until evening of one day. In all probability he received the oil hypo-

2. Cornet, G., and Kossel, H.: Tuberkulose, in Kolle, W., and von Wassermann, A.: *Handbuch der pathogenen Mikroorganismen*, Jena, Fischer 5:391-548, 1913.

3. Lewandowsky, F.: Experimentelle Studien über Hauttuberkulose, *Arch. f. Dermat. u. Syph.* 98:335-398, 1909.

dermically during this time. He had no symptoms from the arm. A few weeks before the present lesion appeared he cut his hand on a cow's horn, and a pyogenic infection ensued with involvement of the regional lymph node (epitrochlear) and much swelling. The tumor then developed in the upper arm (Figs. 6 and 7). Mook and Wander have pointed out that the oil may produce no ill effect until a disturbance of circulatory equilibrium occurs, whereupon granulomatous and foreign-body reaction sets in. As part of the clinical evidence against tuberculosis it should be pointed out that inoculation tuberculosis in the skin always produces a tuberculous lesion at the site of inoculation



Fig. 6.—Rather unsatisfactory photograph of location of lesion. Infiltration covered surface of triceps of right arm.

in addition to the metastatic involvement, and that this metastatic involvement is of the regional lymph nodes rather than of the tissues at large. In this case there was no sign of tubercle in the scar from the trauma.

Treatment.—The treatment employed consisted of wet dressings for a period in order to favor the transition from the inflammatory into the quiescent phase. When the tumid induration and purplish discoloration had disappeared an extensive surgical excision of the affected tissue was performed. The tumid area was allowed to granulate and a skin graft was then made. The therapeutic result so far has been satisfactory.

COMMENT

In view of the probability that a considerable amount of adulterated camphorated oil has been used during the influenza epidemics of the past two years, it would seem that as much medical publicity as possible



Fig. 7.—Infiltration covered surface of upper outer surface of biceps of right arm.

should be given to the camphorated-oil tumor, as its deceptive histology and misleading clinical appearance are likely to result in the diagnosis of tuberculosis and of malignant neoplasia.

THE GENESIS OF NEUROSYPHILIS *

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If abnormalities in the cerebrospinal fluid may be accepted as criteria of early central nervous system invasion in syphilis, the comparatively recent studies carried out by many observers¹ show that such an invasion takes place in from 20 to 35 per cent. of all patients at the time of the first period of generalization of the disease. Earlier clinical surveys of large numbers of syphilitics (notably that of Mattauschek and Pilcz²) demonstrated that approximately the same, or perhaps a somewhat smaller, percentage of untreated or badly treated patients will develop clinical neurosyphilis. These facts have led to the assumption that neurosyphilis of whatever type practically always originates during the first few months of the infection.

The reasons that every case of syphilis is not thus involved probably are to be found, on the one hand, in the protective mechanism against invasion of the nervous system set up by the choroid plexus-meningeal complex, and on the other, in the existence of strains of the organism of syphilis. The consensus of opinion is that a strain of *Spirochaeta pallida* exists which has a definite predilection for nervous tissues, and that most, if not all, of the early neural infections are due to infection with this strain. This opinion is based on the clinical frequency of familial neurosyphilis, and on evidence obtained from experimental animals. However, a study of neurosyphilitic families carried out in this clinic³ has convinced me that not all neurologic infections can be

* From the Syphilis Department of the Medical Clinic, Johns Hopkins Hospital.

1. Fordyce, J. A.: The Diagnostic and Prognostic Significance of Spinal Fluid Findings in Syphilis, *Med. Rec.* **91**:927 (June) 1917. Ellis, A. W. M., and Swift, H. F.: *J. Exper. M.* **18**:162, 1913. Wile, U. J., and Stokes, J. H.: Involvement of the Nervous System During the Primary Stage of Syphilis, *J. A. M. A.* **64**:979 (March 20) 1915. McIver, J.: The Spinal Fluid in Primary and Secondary Syphilis, *J. A. M. A.* **73**:1765 (Dec. 6) 1919. Wile, U. J., and Hasley, C. K.: Involvement of Nervous System During Primary Stage of Syphilis, *J. A. M. A.* **76**:8 (Jan. 1) 1921. Fildes, P.; Parnell, R. J. G., and Maitland, H. B.: Unsuspected Involvement of the Central Nervous System in Syphilis, Publications, Medical Research Committee, London, 1919.

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3. To be published.

traced to a neurotropic strain of *Spirochaeta pallida*; that infection must occasionally, at least, occur from the larger undifferentiated group of organisms without demonstrable tissue tropism; and that in some individuals in whom infection with a probable neurotropic strain does take place, the nervous system may escape invasion entirely.

I have shown ⁴ that the effect of intensive antisyphilitic treatment, even when incomplete, is to reduce the incidence of spinal fluid changes in syphilitic patients without demonstrable neurologic abnormalities to about one-half of that observed in untreated patients. It is also probably true that some patients with early serologic manifestations of neurosyphilis remain clinically well in spite of the spinal fluid changes; in other words, they are able to eradicate the local infection as well as treatment could have done.

TWO GROUPS OF SYPHILITIC PATIENTS

It is possible, therefore, to divide early syphilis into two groups: (1) a group comprising from 20 to 35 per cent. of all cases in which neurologic invasion takes place at the time of, or before the appearance of, secondary manifestations; and (2) the remaining 65 to 80 per cent. in which no such invasion can be demonstrated. Evidence is rapidly accumulating to permit a division of the first group into three subgroups on the basis of response to antisyphilitic treatment, namely, a small proportion who spontaneously deal with the neurologic infection; a fairly large proportion, perhaps about one-half, who are rapidly brought to a serologic normal by routine treatment; and the remainder, whose asymptomatic neurosyphilis is eradicated only with the utmost difficulty, and who probably represent the class of future parenchymatous neurosyphilis.

IMPORTANCE OF TIME OF INVASION

The importance of a clear conception of the time of origin of neurosyphilis is at once apparent when the relations of the disease process to treatment are considered. Does invasion of the central nervous system always take place within the first few months of the infection? If not, may it occur at any time, or only under special late circumstances? If one adheres to the theory that all neurologic infections are early, and may be detected during their asymptomatic stage by the simple procedure of spinal puncture, it would appear feasible to eradicate neurosyphilis almost completely by means of adequate, intelligent treatment. Furthermore, if a negative spinal fluid examination rules out the possibility of the later development of

4. Moore, J. E.: The Cerebrospinal Fluid in Treated Syphilis. J. A. M. A. **76**:769 (March 19) 1921.

neurosyphilis, it is unnecessary to repeat lumbar puncture, and the patient may be dismissed with the positive assurance that he need not fear tabes or paresis.

If, on the other hand, it can be demonstrated that a patient in whom early neurologic signs were absent and whose cerebrospinal fluid examination was negative later did develop neurosyphilis; and if it can be further shown that this contingency may arise under certain definite circumstances, it may be possible to predict the necessity for repetition of lumbar puncture. The development of late neurosyphilis might be determined in two ways: by the appearance of clinical signs of neurologic involvement, or by the demonstration of positive cytobiologic changes later in the course of the disease. Two recent papers have drawn attention to this point. Fordyce⁵ states the question as follows: "The old view that the organism of syphilis may disseminate and invade the central nervous system at any time has nothing to support it except vague clinical impressions. It could only be determined by spinal fluid examinations showing the absence of early infection, and by similar examination in the late stages proving the existence of it. No such proof exists, while all the evidence supports the contrary view." Wile and Marshall,⁶ in discussing the results of 1,869 spinal fluid examinations, state that a negative preliminary puncture followed by positive findings at a later date occurred in only three of the several thousand cases in which puncture was performed. They omit the exact number of patients in whom puncture was repeated once or more.

In common with most observers, we felt until very recently that if negative spinal fluid findings were once obtained, it was unnecessary again to subject the patient to the discomfort of spinal puncture. It is difficult, too, to persuade the average patient in an out-patient clinic to submit to this procedure more than once. The occurrence of the first case shortly to be described stimulated our interest, and fifty-four patients have now been reexamined clinically and serologically. These patients represent all stages of syphilis. In no case was there demonstrable neurologic involvement; a completely negative spinal fluid examination has been obtained in all, usually after from two to four months of treatment. The second lumbar puncture was performed at intervals of from a few months to five years after the first. In fifty-two of these patients, the second spinal fluid examination was

5. Fordyce, J. A.: The Importance of Recognizing and Treating Neurosyphilis in the Early Period of the Infection, *Am. J. M. Sc.* **159**:313 (March) 1921.

6. Wile, U. J., and Marshall, C. H.: A Study of the Spinal Fluid in One Thousand Eight Hundred and Sixty-Nine Cases of Syphilis in All Stages *Arch. Dermat & Syph.* **3**:272 (March) 1921.

completely negative. The histories of the two patients in whom late positive results were obtained are herewith briefly presented, as illustrating two possible ways in which nervous tissue invasions may take place late in the course of the disease.

REPORT OF CASES

CASE 1.—History.—D. B., a colored woman, aged 27, entered the clinic on May 28, 1919, complaining of headache of four weeks' duration. This had come on gradually, and had become very severe, involving chiefly the left side of the

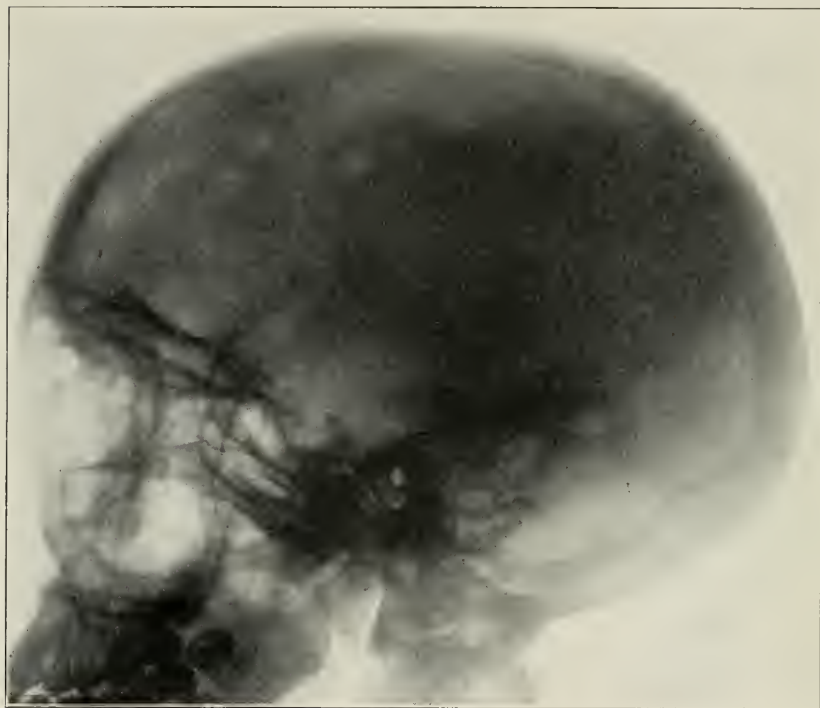


Fig. 1 (Case 1).—Skull, showing multiple areas of bone destruction and gummatous periostitis of inner cranial table.

head and extending down into the face and neck. At first the pain was worse at night, but on admission it was constant and obviously very severe. There was no evidence of syphilis in the marital or the personal history.

Examination.—General and neurologic physical examination failed to disclose any abnormalities except marked tenderness over the whole skull, slight bradycardia, and carious teeth. The sinuses were demonstrated to be clear by transillumination and by roentgenoscopy. The blood Wassermann reaction was positive, and stereoscopic roentgenograms of the skull disclosed numerous areas of circumscribed destruction of the cranial bones, especially in the frontal area, a gummatous periostitis of the inner cranial table (Fig. 1).

Examination of the cerebrospinal fluid on admission revealed no cells, a negative globulin test, negative Wassermann reaction with quantities ranging from 0.1 to 1 c.c., and negative colloidal tests.

Treatment.—After the first dose of arsphenamin, on June 2, there was marked intensification of the headache, amounting to agony, for two days (Herxheimer reaction). This rapidly improved, and ten days after the beginning of treatment, it had completely disappeared. Between June 2 and July 3, she received six doses of arsphenamin. The Wassermann reaction of the blood was persistently positive, but changed to negative by July 23. Mercury by inunction with potassium iodid was then used for seven weeks. The second course of six doses of arsphenamin was given from September 4 to October 27, after which the patient was again placed on rubs. The blood Wassermann reaction had remained negative.

In spite of faithful application to treatment, on November 27 the patient suddenly developed a complete right facial paralysis. The eighth nerve was not involved, and no other neurologic abnormalities were demonstrable. A repetition of the lumbar puncture on December 2, five days after the onset of the facial paralysis, yielded these results: 112 cells, globulin strongly positive, and Wassermann reaction positive with 0.2 c.c. Unfortunately colloidal tests were not made. The blood Wassermann reaction was again negative. Immediate resumption of arsphenamin caused the paralysis to clear up in six weeks, and the spinal fluid on Aug. 7, 1920, was again completely negative.

COMMENT

This case bears a superficial resemblance to the class of neurorecidives, but differs in several important points. Neurorecidives usually occur early in the course of syphilis and after a lapse in treatment. Judging by the extent of bone destruction in the lesion, this was a case of late syphilis, which would ordinarily be classed as tertiary. Presumably the disease had existed for some time, probably for more than a year. No lapse in treatment had occurred; indeed, the patient was remarkably faithful in carrying out all instructions. Furthermore the theory of the genesis of neurorecidives includes the presence of organisms in the nervous system from the time of the first period of generalization of the disease. In this patient, the original negative spinal fluid examination would seem to rule out this possibility. The evidence presented warrants the probable conclusion that invasion of the nervous system took place by direct extension from the bone lesion, perhaps at the time of the Herxheimer reaction heretofore referred to.

CASE 2.—History.—J. B., a white man, aged 23, contracted a chancre about Feb. 15, 1919. When he reported for examination on March 25, he showed an indurated scar on the inner lamella of the prepuce, extreme satellite adenopathy, general glandular enlargement, and a profuse macular rash. The blood Wassermann reaction was positive.

Treatment.—His first course of arsphenamin consisted of six doses given at weekly intervals from March 25 to May 6. The blood Wassermann reaction

became negative after the fourth injection, and his spinal fluid, examined on May 29, two weeks later, after he had begun to use mercury by inunction, showed no cells and negative globulin, Wassermann and colloidal tests.

He was kept on rubs until July 15, from which time until August 26 five more doses of arsphenamin were given. A provocative Wassermann reaction was obtained in the blood after the first injection of this series, but the test promptly became negative again.

From August 26 till December 5 the patient remained away from the clinic, and for these fourteen weeks took no treatment. He returned with recurrent mucous lesions on the penis and the recurrence of a positive Wassermann reaction. From this time until the present, treatment has been persisted in though somewhat irregularly. During the eleven months following his return he received twenty injections of arsphenamin in three courses, with interim mercury for sixteen weeks. The blood Wassermann reaction again reverted to negative after the fifth arsphenamin treatment and remained so. The mucous lesions healed promptly, and he had no further symptoms of any kind.

On Nov. 8, 1920, spinal puncture was repeated. There were 37 cells, strongly positive globulin test, positive Wassermann reaction with 0.2 c.c., and paretic colloidal gold and mastic curves. During the course of arsphenamin which followed this puncture, the blood Wassermann reaction again became positive.

COMMENT

Here is a patient in whom the early puncture demonstrated the probable freedom of the central nervous system from involvement. During a lapse in treatment, there was a fresh generalization of the disease, manifested by recurrent secondary lesions and a recurrent positive Wassermann reaction in the blood. Presumably it was during this period of fresh generalization that invasion of the nervous tissue took place.

It may be objected that in both of these patients early invasion of the nervous system had taken place, and that the late positive results in the spinal fluid were in the nature of a provocative reaction, as described by Solomon and Klauder.⁷ The presence of definite opportunity for fresh invasion in both of these cases is against such a theory.

A distinction must be drawn between purely vascular neurosyphilis and the meningeal, parenchymatous, and mixed types. It is fairly common, in the course of a generalized vascular involvement, to have neurologic manifestations due to thrombosis or hemorrhage from damaged cerebral vessels; and this may occur in the complete absence of other evidence of nervous tissue invasion. If this be regarded as a form of neurosyphilis, rather than as generalized syphilitic vascular disease, it must be admitted that it can arise at any time during the course of the infection, and that it usually does not betray its existence by early changes in the spinal fluid.

7. Solomon, H. C., and Klauder, J. V.: Provocative Reactions in the Cerebrospinal Fluid in Neurosyphilis, *Arch. Dermat. & Syph.* **2**:679 (Dec.) 1920.

For the meningeal, parenchymatous, and mixed forms of neurosyphilis, on the other hand, four possible modes of origin appear. Invasion of the central nervous system may take place at any time, the older theory for which, as Fordyce points out, no justification exists. It usually occurs early in the course of syphilis, during the first period of generalization of the disease. But a nervous system which has escaped this early invasion may be involved at a later date, either by direct extension from a neighboring focus of syphilitic disease, or by an actual fresh invasion during a second or later period of generalization and spirochaetemia.

SUMMARY

1. In fifty-four cases of syphilis in all stages of the disease, but without demonstrable neurologic involvement, an early negative spinal puncture was repeated, with positive results in two.

2. In one of the positive cases, invasion of the central nervous system had apparently taken place by direct extension from a gummatous periostitis of the inner cranial table; in the other, it probably occurred during a second period of generalization of the disease.

3. In the majority of cases of neurosyphilis, invasion of the central nervous system takes place during the first few months of the infection; but in some cases it may occur at any time during the course of syphilis by one of the two mechanisms outlined.

4. The appearance of recurrent secondary syphilis or the recurrence of a positive blood Wassermann reaction after a lapse in treatment is the probable outward manifestation of a fresh generalization of the disease, and should be made the occasion for reexamination of the cerebrospinal fluid.

INTERNAL POISONING FROM RHUS

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ETIOLOGY

Most cases of internal poisoning by rhus have been caused by chewing the leaves of the plants and swallowing the juice in order to attain immunity to the poison. One of these cases terminated fatally (Alumbaugh,¹ 1903). Dakin² (1829) aptly commented on this procedure nearly a century ago:

Some good meaning, mystical, marvellous physicians, or favored ladies with knowledge inherent, say the bane will prove the best antidote, and hence advise the forbidden leaves to be eaten, both as a preventive and cure to the external disease. I have known the experiment tried, which resulted in an eruption, swelling, redness and intolerable itching, around the verge of the anus.

In 1907, Conner³ reported one case caused by thoughtless chewing of a tender shoot of *Rhus toxicodendron*. Two cases are recorded in which children were poisoned by eating the fruit of *Rhus toxicodendron* (Moorman⁴ 1866). Root infusions were cited as a cause by French⁵ in 1903.

In internal rhus poisoning the amount of poison ingested is generally larger than in rhus dermatitis. There is also a possibility of other poisons than that which is the principal cause of dermatitis being absorbed from the plant.

The unripe fruits of *Rhus toxicodendron* and *Rhus diversiloba* produce dermatitis, but when fully ripe they do not cause dermatitis (McNair,⁶ 1917). The latter fact does not prove that the fruit is not poisonous when swallowed.

The fruit of *Rhus coriara*, a plant listed among the nondermatitis-producing rhus, will produce severe poisoning when swallowed (Esca-

1. Alumbaugh, W. E.: Med. World **21**:176, 1903.

2. Dakin, R.: Remarks on the Cutaneous Affection Produced by Certain Poisonous Vegetables, Am. J. M. Sc. **4**:98, 1829.

3. Conner, J. J.: Poisoning by Rhus Toxicodendron, J. Dermat. **11**:368, 1907.

4. Moorman, J. W.: Poisoning by Eating the Fruit of Rhus Toxicodendron, Am. J. M. Sc. **51**:560, 1866.

5. French, J. M.: Rhus Toxicodendron and Rhus Poisoning, Merck's Arch. **5**:223, 359, 1903.

6. McNair, James B.: Fats from Rhus Diversiloba and Rhus Laurina, Botanical Gaz. **64**:330, 1917.

fet,⁷ 1847). The symptoms of children who had swallowed the seeds were similar to those cited in the cases of the two children who ate the fruit of *Rhus toxicodendron* reported by Moorman. In cases of poisoning caused by both these fruits the patients became drowsy and stupid and in a short time vomited partially digested fruit and fluid the color of wine. Convulsions followed.

Orfila,⁸ in 1866, carried on a series of experiments on dogs with an aqueous extract of *Rhus radicans*. In some cases fatal results followed the ingestion of the extract, its injection into the jugular vein, or its application to a wound in the leg. The application of the extract to the cellular tissue on the back of a dog produced no "remarkable phenomena." The principal irritant of *Rhus radicans* is practically insoluble in water. The poison in the aqueous extract may have been tannin.

COURSE OF INTERNAL RHUS POISONING

The features of internal rhus poisoning which are similar to those of rhus dermatitis are the shortness of its course and, typically, its differentiation into stages. The following stages in their proper sequence are generally recognized:

Stage of Infection.—This stage covers the period of time required by the poison to enter the outer surface of the mucous membrane and lining tissues in the mouth, throat and alimentary tract.

The Stage of Latency.—This stage covers the period of time in which the poison continues to enter the tissues up to the point of the production of symptoms. In a case in which poisoning occurred through the inhalation of smoke from burning rhus an irritation of the throat was immediately noticed (Seabrook,⁹ 1891). In the cases of two children, one 6 and the other 8 years of age, who had eaten fruit of *Rhus toxicodendron*, symptoms of drowsiness appeared in a few hours (Moorman, 1866). In a case in which a young shoot of *Rhus toxicodendron* had been thoughtlessly chewed, symptoms of burning and itching of the lips and mouth were evident in about twenty-four hours (Conner, 1907). This and other evidence at hand proves that the symptoms of internal rhus poisoning become evident in a shorter length of time than in the average cases of external poisoning. The stage of latency, therefore, is an appreciably limited one, and its duration is a matter of a few hours at most when a considerable quantity

7. Escafet: De l'action toxique des baies du *Rhus coriaria*, Sumac des corroyeurs. Empoisonnements avec terminaisons funeste, J. de chim. méd. **3**: 197, 1847.

8. Orfila, A. J. B.: Traité de toxicologie **2**:132, 1866.

9. Seabrook, H. H.: A Peculiar Case of Poisoning, New York M. J. **54**: 51, 1891.

of poison has been ingested. During the time of ripening the fruits of *Rhus diversiloba* and *Rhus toxicodendron* contain an increasing amount of fat which has a maximum of about 20 per cent. (McNair, 1917) in the mesocarp. As the irritant poison is soluble in this fat, the fat may aid in the absorption of the poison. Fat absorption, however, is mainly a function of the intestines, whereas the poison produces stomatitis and gastritis, as well as enteritis.

Stage of Prodromes.—In this stage vague symptoms appear, such as headache, lassitude and possibly some irritation about the point of entrance of the poison. These prodromal symptoms are usually of brief duration; the duration depends on the same general factors that are indicated in the preceding stage. In a case of poisoning by the inhalation of smoke from burning rhus, irritation of the throat and general malaise occurred within a day after exposure. In a case of poisoning, probably caused by rhus smoke coming through an open car window, a sensation similar to sunburn was noticed in about twenty-four hours. Symptoms developed in a case of stomatitis in about the same length of time.

Stage of Invasion.—In this stage the symptoms characteristic of the disease make themselves manifest. As in rhus dermatitis, two types are recognized, namely, a frank or sudden invasion and an insidious or gradual invasion. The former is, doubtless, due to a sudden and severe intoxication, while the latter is due to a more gradual action. When the frank invasion occurs, naturally this stage is well separated from the prodromal, but they gradually merge during the insidious invasion. One of several factors may account for a frank invasion: 1. Poison swallowed in a large amount comes in contact with a large surface. Although it may be slowly absorbed, much is absorbed at the same time. 2. Some very sudden cause may be operative in reducing the vitality of the person, so that a given volume of poison may have an extreme and sudden effect. 3. The poison may have accumulated in a given focus owing to defective drainage, and then, by a sudden discharge of the poison into the system, a large quantity may be absorbed.

Primary Effect.—The primary effect of poisoning in this stage is to stimulate one or more functions of the system, while the secondary or final effect is to depress or pervert such functions subsequent to the production of degenerative and necrotic changes. Practically every function may be affected and metabolic and circulatory activity may receive an especial stimulus. Either with or without a direct effect on the thermogenic centers, the excessive metabolic activity is liable to increase the body heat as well as to increase the

amount of waste products. The effect on the circulatory system is equally striking; this consists of increased cardiac force and vasoconstriction, as shown in a rise of blood pressure. In the frank invasion there is not only a suddenness of onset of symptoms, but also great severity of symptoms. Internal rhus poisoning may be ushered in by some special phenomena, such as nausea and vomiting, followed by convulsions when the poison acts on the central nervous system. Children are more likely to show the latter effects than adults.

Effects are noted in several parts of the body:

Abdominal Area.—This shows distinct congestion. In the gastrointestinal tract increased peristalsis and diarrhea may be caused. Nausea is common. Intense congestion of the kidneys may cause a diminished output of urine, while slight congestion may somewhat increase the amount.

Pulmonary Area.—This area likewise is congested. Dyspnea is induced by nervous influences and perhaps by a reduction in the air space of the lungs due to congestion. A burning in the throat and a dry hoarse cough may occur.

Cerebral Area.—This area is so closely associated with the large vascular trunks that it shares in the congestion. A feeling of fulness and headache, of greater or less severity, is likely to develop.

The pupils are dilated. The face is usually flushed.

Stage of Acme.—This is in reality but a continuation of the last stage, and is not clearly differentiated from it. The lesions of this period are dependent on congestion, increased metabolism and degenerative changes. Naturally, extension of an inflammatory process may occur by continuity of structure. For instance, in a case of rhus proctitis and vulvitis (Dunmire,¹⁰ 1881), peritonitis developed with "great pain and tenderness over the bowels, particularly on the left side, which afterward extended over the abdomen. The slightest pressure would produce pain." At the beginning of the stage of acme, stimulation of the functions occurs, together with congestion and febrile disturbances.

Amphibolic Stage.—This is the sequel of the preceding stage, and is not clearly differentiated from it. It is the wavering stage, for at this time the symptoms are often changeable, and there may be a sudden rise or fall of temperature. If, at this time, the protective powers of the body are sufficient to combat successfully the action of the poison, a reduction of temperature will occur and the disease will decline. Conversely, if the poison proves to be the stronger, the patient finally succumbs to the process. Only one death is recorded

10. Dunmire, J. B.: A Case of Proctitis and Peritonitis from Rhus Poisoning of the Buttocks, Philadelphia Med. Times **12**:636, 1881-1882.

from internal rhus poisoning. A patient suffering from rhus dermatitis chewed some *Rhus toxicodendron* leaves to produce immunity; he died two days later (Alumbaugh, 1903). If death does not take place in this stage, it is followed by the stage of decline.

Stage of Decline.—In this stage the symptoms which are directly due to the poison disappear, while those incident to the degeneration, inflammatory and metabolic disturbances may persist.

Stage of Convalescence.—The disease itself has now disappeared, but this stage represents the attempt at restitution of the body structures. The length of this period and the ability of the system to recover completely from the effects of the disease are dependent on age, nutrition, sanitary surroundings and other conditions. Other diseases may develop during this period due to depression of vitality, but I have found no record of sequelae or relapses that have occurred in persons poisoned internally by rhus.

THE SACHS-GEORGI TEST FOR SYPHILIS *

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Practically ever since the discovery of the Wassermann ¹ reaction, investigators have endeavored to devise some simpler test which would give equally satisfactory results, and which, besides being of practical importance, might throw some light on the mechanism of the Wassermann reaction. Most of them have endeavored to accomplish this by various precipitation methods. The theory that the formation of a precipitate occurs in a positive Wassermann reaction was formulated by Michaelis, ² Levaditi and Yamanouchi, ³ Elias, Neubauer, Porges and Salomon, ⁴ and by Liefmann. ⁵

In 1907, Fornet and Schereschewsky ⁶ obtained what they believed to be specific precipitates by using the serums of patients with active syphilis as precipitinogen and the serums of patients with paresis as precipitin; they also used saline extracts of syphilitic livers as precipitinogen, but, while they obtained precipitates with these, they also obtained them by using normal liver extracts. In the same year, Michaelis ² tried precipitin reactions, using saline extracts of syphilitic livers as antigen.

Klausner, ⁷ in 1908, asserted that the addition of distilled water to serums gave precipitates with syphilitic, but not with normal, serums. Also in 1908, Porges and Meier ⁸ used solutions of lecithin and sodium glycocholate to obtain precipitates with syphilitic serums; following them, Elias, Neubauer, Porges and Salomon ⁹ devised a method, utilizing sodium glycocholate.

* From the Department of Bacteriology, College of Physicians and Surgeons, Columbia University.

1. Wassermann, Neisser and Bruck: *Deutsch. med. Wchnschr.*, 1906, No. 19, p. 745.

2. Michaelis: *Berl. klin. Wchnschr.*, 1907, No. 46, p. 1477.

3. Levaditi and Yamanouchi: *Compt. rend. Soc. de biol.* **59**:740, 1907.

4. Elias, Neubauer, Porges and Salomon: *Wien. klin. Wchnschr.*, 1908, No. 21, p. 748.

5. Liefmann: *München. med. Wchnschr.*, 1909, No. 41, p. 2097.

6. Fornet and Schereschewsky: *Berl. klin. Wchnschr.*, 1908, No. 18, p. 874.

7. Klausner: *Wien. klin. Wchnschr.*, 1908, No. 7, p. 214.

8. Porges and Meier: *Berl. klin. Wchnschr.*, 1908, No. 15, p. 731.

9. Elias, Neubauer, Porges and Salomon: *Wien. klin. Wchnschr.*, 1908, No. 23, p. 831.

In 1909, Jacobsthal,¹⁰ by means of the ultramicroscope, showed that a precipitate was formed in a mixture of syphilitic serum and Wassermann antigen after one-half hour's incubation.

Bruck and Hidaka in a postscript to a paper by Bruck and Stern,¹¹ in 1910, say that after mixing an alcoholic extract of a syphilitic liver and serums, and letting this mixture stand for twenty-four hours, the Wassermann positive serums showed precipitates, whereas the negatives never did. Ternuchi and Toyoda,¹² in this year, using "cuorin," asserted that with this they obtained a precipitate with syphilitic, but not with normal, serums.

In 1911, Hermann and Perutz¹³ used cholesterinized solutions of sodium glycocholate to cause precipitates with syphilitic serums.

Lange,¹⁴ in 1912, devised his now familiar colloidal gold test for spinal fluids.

Bruck¹⁵ published a "serochemical" method for the diagnosis of syphilis in 1917, which depended on the different solubilities in distilled water of precipitates formed by the addition of nitric acid and distilled water to serums. In the same year, Meinicke¹⁶ brought out his reaction, in which he tested the solubilities in various concentrations of sodium chlorid, of precipitates formed between serums and Wassermann antigen. Vernes,¹⁷ in this year, published his method of using colloidal ferric hydroxid and serums.

In 1918, Sachs and Georgi¹⁸ gave out their method, which we give in detail.

Guillain, Laroche and Lechelle,¹⁹ in 1920, used a colloidal suspension of benzoin in the diagnosis of spinal fluids.

Of the methods mentioned, those of Meinicke and Sachs and Georgi appear the most promising, and, during the last two years, have received a great deal of attention, especially by German workers, Sachs and Georgi²⁰ in a recent article giving forty-nine references to articles on

10. Jacobsthal: München. med. Wchnschr., 1909, No. 50, p. 41.

11. Bruck and Stern: Ztschr. f. Immunitätsforsch. u. exper. Therap. **6**:592, 1910.

12. Ternuchi and Toyoda: Wien. klin. Wchnschr., 1910, No. 25, p. 919.

13. Hermann and Perutz: Med. Klin., 1911, No. 2, p. 60.

14. Lange: Berl. klin. Wchnschr., 1912, No. 19, p. 897.

15. Bruck: München. med. Wchnschr., 1917, pp. 1-40 (quoted from abstract in J. A. M. A., 1917, p. 944, as the original article was not available).

16. Meinicke: Berl. klin. Wchnschr. **54**:613, 1917 (not available), and 1918. No. 4, p. 83.

17. Vernes: Compt. rend. Acad. d. sc., 1917, 165, p. 769.

18. Sachs and Georgi: Med. Klin., 1918, No. 33, p. 805.

19. Guillain, Laroche and Lechelle: Bull. et mém. Soc. méd. d. hôp. de Par. **44**:33, 1920 (not available; quoted from abstract in J. A. M. A. **76**:208, 1921).

20. Sachs and Georgi: Arb. aus dem Institut f. Exp. Therap. u. dem Georg Speyer-Hause zu Frankfurt A. M. **10**:5, 1920.

these reactions appearing mostly in 1919, a few in 1918—all in the German literature. On the whole, the agreement of the Sachs-Georgi test with the Wassermann has been very satisfactory. Sachs and Georgi, in the article published in 1920, report the results, both their own and those of other workers, on 12,124 parallel Wassermann and Sachs-Georgi tests, with an agreement in 92.44 per cent., the Sachs-Georgi test being negative or doubtful where the Wassermann was positive or doubtful in approximately 3 per cent., and positive where the Wassermann was doubtful or negative in approximately 7 per cent. Meyeringh,²¹ in a recent publication, comparing the Wassermann, Sachs-Georgi and Meinicke tests on 303 specimens of blood, found the Wassermann reaction positive in 30.6 per cent., the Sachs-Georgi in 32.31 per cent., and the Meinicke in 36.63 per cent. Also in 1920, Messerschmidt²² reported on 1,100 comparative Wassermann and Sachs-Georgi reactions with an agreement of 85 per cent., Kirschner and Segall²³ on over 1,000 similar tests with an agreement of 80 per cent., and Baumgärtel²⁴ on 7,000 such tests with a 90 per cent. agreement. In this country, Hull and Faught,²⁵ using a considerably modified technic, reported on 296 cases with an agreement of 88 per cent.

We decided to try the Sachs-Georgi test and to compare it with the Wassermann reaction, not attempting to control the tests by the clinical aspects of the cases, as our primary interest in the test was its relation to the Wassermann reaction, rather than its value in the diagnosis of syphilis.

THE SACHS-GEORGI REACTION

Technic.—Our technic is essentially that of Sachs and Georgi with one variation, as noted in the following:

Extract.—A beef heart is freed from fat, endocardium and large blood vessels, and is cut up fine in a meat chopper. It is then ground in a mortar with sand. After this it is mixed with 5 volumes of alcohol (95 per cent.) and shaken vigorously for from four to five hours in a shaking machine, with a few glass beads added. It is then allowed to stand over night at room temperature, is filtered through ordinary filter paper next morning and placed in the icebox for at least two days; at the end of this time it is filtered again through filter paper to remove the precipitate that comes down in the cold. It is now ready for use and is stored at room temperature. Before using it in the test, it must be titrated against a standard extract as follows:

21. Meyeringh: *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **30**:51, 1920.

22. Messerschmidt: *Deutsch. med. Wchnschr.*, 1920, No. 6, p. 150.

23. Kirschner and Segall: *Wien. klin. Wchnschr.*, 1920, No. 18, p. 377.

24. Baumgärtel: *München. med. Wchnschr.*, 1920, No. 15, p. 421.

25. Hull and Faught: *J. Immunol.*, 1920, No. 6, p. 521.

Given quantities (say 10 c.c.) are diluted with 1, 2 and 3 volumes of alcohol (95 per cent.). To four portions of each of these dilutions are then added 0.03 per cent., 0.045 per cent., 0.06 per cent. and 0.075 per cent. of a 1 per cent. alcoholic solution of cholesterin. These various cholesterinized portions are diluted with 5 volumes of normal saline, and set up with a series of positive and negative serums against a standard extract; that dilution and that amount of cholesterin is chosen for use in the tests which best agrees with the standard. Of course, the amounts of cholesterin may have to be varied from those given in the preceding. We have used our extracts diluted with 2 volumes of alcohol and with the addition of 0.06-0.07 per cent. of the 1 per cent. cholesterin solution. Sachs and Georgi say that most of their extracts have been satisfactorily diluted with 2 volumes of alcohol with the addition of 0.045 per cent. to 0.06 per cent. of the cholesterin solution. At least two such extracts should be used in each test.

Serum.—The serum should, as in the Wassermann reaction, be as fresh as possible, although a reasonably old serum (3 or 4 days) is apparently quite satisfactory. A small amount of hemoglobin does not interfere. The serum is inactivated at 55 to 56 C. for one-half hour, and we have always allowed at least three hours to elapse from the time of inactivation to use in the test, as Münster²⁶ has shown that serums used immediately after inactivation may give doubtful, unspecific reactions.

Saline Solution.—Eighty-five one-hundredths per cent. of sodium chlorid in distilled water is used. This solution should be sterile and as freshly made as possible.

TEST

Serum.—One-tenth cubic centimeter of serum is added to each tube, and to this is added 0.9 c.c. of the normal saline. At least three tubes should be set up on each specimen of serum, one for each antigen and one for the serum control. (We used tubes approximately 10 by 1.2 cm.) •

Extract.—To each tube to be tested is added 0.5 c.c. of the extract dilution, made in the following manner:

The extract is to be diluted with 5 volumes of saline and the results of the tests depend largely on the manner in which this dilution is made, as was shown to hold true for the Wassermann reaction by Sachs and Rondoni²⁷ in 1908. If the saline is added rapidly, all at one time, the resulting dilution will be only slightly opalescent and not sensitive enough; if the saline is added too slowly, the extract will become very cloudy and will either tend to precipitate out by itself or will be too sensitive. In attempting to employ a standard method which would eliminate the personal equation as much as possible, following a suggestion of Sachs and Georgi, we carry out the dilution as follows: The required amount of extract is placed in an Erlenmeyer

26. Münster: München. med. Wchnschr., 1919, No. 19, p. 505.

27. Sachs and Rondoni: Berl. klin. Wchnschr., 1908, No. 44, p. 1698.

flask. To it from a buret is rapidly added an equal volume of saline; the mixture is shaken gently and is allowed to stand ten minutes; then the remaining 4 volumes of saline are rapidly run in; the mixture is again shaken gently, and the extract is then ready for use. (At first we let it stand an hour before adding it to the serums, but later found this to be unnecessary.)

Serum Control.—To one of the tubes of each serum as set up in the foregoing is added 0.5 c.c. of alcohol diluted with 5 volumes of saline. If this tube shows any definite precipitate, the serum is unsuitable for the test and another specimen must be obtained. (We have never seen such a precipitate.)

Extract Controls.—Five-tenths c.c. of each extract dilution is mixed with 1 c.c. of the normal saline. These tubes should show no precipitate or granular appearance if the extract dilution is satisfactory.

Incubation.—All the tubes are thoroughly shaken and placed in the incubator at 37.5 C. for twenty hours. They are then read and allowed to stand for twenty hours more at from 14 to 18 C. or in the icebox. After this time, the final readings are taken.

Readings.—Negative and positive reactions are read with the naked eye, and present appearances similar to bacterial agglutination or precipitin tests. The strongly positive reactions show a heavy, flocculent sedimented precipitate with a clear supernatant fluid, which sometimes contains a few flocculi; the moderately positive reactions show a diffuse but very definite finely flocculent precipitate, often with some sediment; the weak positive reactions show the same to a lesser degree. Shaking the tubes and reading against a dark background often helps in the weak tests. If a test looks suspicious, but is not definite, it may be centrifuged at moderate speed for a few minutes, then shaken and read; if such a test is positive, on shaking after centrifuging, a few whitish, compact flocculi will rise from the bottom of the tube; if negative, no such flocculi will be seen, but a slight, grayish sediment may be found, which, on shaking, is dispersed into the supernatant fluid, becoming invisible.

Sachs and Georgi in a description of their technic say the tests should be read with Kuhn and Woihe's agglutinoscope, but we have not found this necessary. Meyer²⁸ has shown that the reaction may be hastened by centrifuging the tests after letting them stand a few hours, as shown by Bruck and Hidaka¹⁵ in their tests. Hull and Faught²⁵ state that if the tests are centrifuged immediately after adding the extract dilutions, they can be read then, and the same results will be obtained as when the tests are read after standing twenty-four hours.

The principal variation in our technic from Sachs and Georgi's is our method of incubation. We based our method on their suggestions as the result of Neukirch's²⁹ work. In the original Sachs-Georgi reaction, the tubes were incubated for two hours at 37.5 C. and then allowed to stand at room temperature for from eighteen to twenty hours, but the results so obtained were sometimes unspecific, especially if the room temperature was low, false positive reactions occurring; if, on the other hand, the incubation period was twenty hours in the

28. Meyer: Berl. klin. Wchnschr., 1919, No. 14, p. 331.

29. Neukirch: Arb. aus dem Institut f. Exper. Therap. u. Georg Speyer-Hause zu Frankfurt A. M. 10:49, 1920.

incubator, the results, while strictly specific, were not sufficiently sensitive. Neukirch showed that an incubation period of twenty hours in the icebox following the twenty hours in the incubator brought out the weak positive reactions; also, that if the first incubation was carried out in the icebox, all the true positive and many other false positive reactions appeared; however, if twenty hours at 37.5 C. followed this, the nonspecific precipitates disappeared, leaving only the specific reactions.

AUTHORS' RESULTS WITH SACHS-GEORGI AND WASSERMANN TESTS

TABLE 1.—COMPARISON OF RESULTS WITH SACHS-GEORGI AND WASSERMANN TESTS

Number of Tests	Agreement		Percentage	Differ.	
	+	—		Sachs-Georgi —, Wassermann +	Sachs-Georgi +, Wassermann —
520	164	320	93.07	34	2

TABLE 2.—RESULTS WITH WASSERMANN AND SACHS-GEORGI TESTS

Number of Tests	Wassermann		Sachs-Georgi						Per-centage
	Cholesterin Antigen	Alcoholic Antigen	++++	+++	++	+	+*	—	
79	++++	++++	50	17	10	2	0	0	100
13	Cholesterin > Alchohol								
10	++++ or +++	+++ or ++	3	4	3	2	0	1	92
8	++++ or +++	+ or —	1	3	2	3	0	1	90
	++++	++++	0	1	2	4	0	1	87
	Cholesterin < Alchohol								
22	+++ or ++	++++ or +++	2	4	4	8	0	4	81
22	+ or —	++++ or +++	0	3	4	6	5	4	81
2	++	++	0	0	1	0	0	1	50
	Cholesterin > Alchohol								
23	++ or +	+ or —	0	0	5	5	5	8	65
	Cholesterin < Alchohol								
15	+ or —	++ or +	0	0	0	2	3	10	53
4	+	+	0	0	0	0	0	4	0
198	56	32	31	32	13	34	

* Suspicious, centrifuged; proved positive on centrifuging.

The Wassermann tests with which we compared our results were carried out in Dr. J. G. Hopkins' laboratory, and were done with one cholesterin antigen and incubation at 37.5 C., and with two alcoholic antigens with icebox incubation.

We have tabulated our results in some detail as they appear to be of sufficient interest, as the comparison of the degree of positiveness and type of antigen is important from the practical standpoint and from the theoretical as throwing some light on the question as to whether the two reactions depend on the same factor or factors. No direct proof has as yet been given in answer to this. We have also tabulated the results with the cholesterin and alcoholic antigens separately as they at times show such a difference.

As will be seen from Table 1, the Wassermann reaction was positive in thirty-four cases in which the Sachs-Georgi reaction was negative;

in two cases, the Sachs-Georgi reaction was weakly positive while the Wassermann reaction was negative, both these cases occurred in treated syphilitic patients; we at first tried to obtain records on some of the thirty-four cases, but found them so incomplete that it was useless. As will be seen, the Sachs-Georgi test is by no means always strongly positive when the Wassermann reaction is strongly positive; although it is rarely negative in such cases. In a few cases, the Sachs-Georgi reaction shows a similar degree of positiveness with the weak and strongly positive Wassermann reactions, but on the whole, the degree of positiveness corresponds roughly, except in one group of cases, in which, with the Wassermann test, the cholesterin antigen was + or — and the alcoholic antigen was ++++ or +++; such reactions are noteworthy in view of the fact that a cholesterinized antigen is generally thought to be more sensitive than a simple alcoholic antigen and might justly make one suspicious of their specificity. There were twenty-two cases in this group, the Sachs-Georgi giving four negative reactions and five + reactions, whereas in ten cases in which the cholesterin antigen was ++++ or +++, and the alcoholic + or —, there were no + results, and only one negative. Again in the group in which the alcoholic antigen was ++ or + and the cholesterin + or —, the alcoholic being stronger in each instance, the agreement of the Sachs-Georgi was 33 per cent., whereas in the group in which the results were the reverse, the agreement was 65 per cent. It might be argued that the greater agreement of the Sachs-Georgi test with the cholesterin antigen in these two groups depended on the fact that these antigens were more similar, both being cholesterinized, but this objection would not appear to hold as the agreement with the total number of positive reactions caught by the cholesterin antigen was 85.7 per cent., and with the alcoholic 86.6 per cent.

CONCLUSIONS

On looking over the results as a whole, it will be seen that the Sachs-Georgi test, as done by this method, gives no unspecific positive reactions as controlled by the Wassermann test, and that it does not give as many positive reactions, especially when the Wassermann reactions are weak or doubtful; whether this last fact is an advantage or not, can only be decided by doing a large number of tests on cases which can be carefully controlled clinically. Its great simplicity, the great saving in materials and the encouraging agreement with the Wassermann test, certainly make it worthy of further study, especially when the clinical aspects of the cases can be determined. Whether it will supplant the Wassermann test is still a question, but it appears to

be of value in its present status for confirming doubtful or disputed Wassermann reactions, and to be of use when the materials necessary for Wassermann tests are not available.

SUMMARY

1. The Sachs-Georgi reaction agreed with the Wassermann reaction in 93.07 per cent. of 520 parallel cases.

2. As performed by the method described, the Sachs-Georgi test gives no unspecific positive reactions as controlled by the Wassermann test, and also does not give as many positive reactions, especially in cases in which the Wassermann reaction is weak or doubtful.

3. Because of its simplicity and apparent dependability, it deserves further study, especially in cases in which the clinical aspects can be definitely determined.

A COMPARATIVE STUDY OF SYPHILIS IN WHITES AND IN NEGROES *

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Variations in the reaction of persons to syphilitic infection have caused much speculation. Fifty years ago Fournier emphasized the impossibility of predicting the course of a syphilitic infection. Even today we can offer a prognosis only on the basis of efficient treatment.

Quoting Krause,¹ "two really fundamental factors can possibly have an influence on disease. These are inheritance, or the nature and activities of tissues as born into the world; and environment, which includes every mundane experience which, directly or indirectly, may have an effect on the constitution and function of tissues."

Inheritance probably explains in part certain differences in tissue reactions in syphilis, such as the early development of allergy in syphilis maligna, and the apparent absence of such a process in syphilis secundaria tarda. Inherited differences may have a determining influence on the localization of syphilitic lesions in various tissues or on the character which these processes assume.

Environment, employed in its broadest sense, embraces numerous considerations. It includes occupation, habits, associated disease and the effect of treatment. The latter is obviously of paramount importance in influencing the course of syphilis, when we consider the powerful antisyphilitic action of the drugs employed, with their varied chemical composition and their fundamental differences in mode of action on spirochetes and on syphilitic processes.

In syphilis there may be added as an additional influence on the course of the disease, variations in strain of *Spirochaeta pallida*, a conception long suggested by clinical observation and apparently substantiated by recent animal experimentation. It is, however, hardly conceivable that strains infecting the negro differ from those harbored by whites, except in so far as racial antipathy and the legal restrictions placed on miscegenation prevent intimate personal contact between the races and pave the way for the evolution of strain variations. It should

* From the syphilis department of the medical clinic, Johns Hopkins Hospital.

1. Krause, A. K.: Environmental Factors in Tuberculosis, Am. Rev. Tuberc., 4:717 (Nov.) 1920.

be stated that not all syphilologists accept the existence of strains of *Spirochaeta pallida*, and more convincing proof must be adduced before the question can be definitely settled.

In this paper a comparative study of syphilis in whites and in negroes is undertaken for the purpose of emphasizing inherited racial differences in response to syphilitic infection. It is evident that inheritance and environment are closely interdependent. Environmental conditions may be immediately responsible for the bringing to light of inherited tendencies. There are, however, certain clinical characteristics of syphilis in the negro which can hardly be explained on grounds other than inherited biologic differences.

Racial differences in syphilis have been studied chiefly in the former German colonies, in the North African possessions of the French, and in the negro of the United States. Pertinent also are Neisser's² experience among the Malays and Chinese of Java, von Düring's³ statistics from Asia Minor, and Lambkin's⁴ report to the British Government on Syphilis in Uganda.

Neisser states that racial differences are not improbable and cites the results of Rotschuh in Central America, who found that syphilis assumed a milder form in the Indian population than in white patients and negroes. Though Neisser's experience in Java gave him the impression that syphilis was most severe among white people and least severe among Malays, he found no clinical differences between the disease as it existed in Java and that observed in Germany. In his opinion the apparent severity does not depend on a special type of syphilis, but rather on the effects on the whites of climate, gastrointestinal disease, malaria and alcoholism. Such an explanation seems reasonable for the supposedly severe course of syphilis acquired by whites in tropical climates.

That syphilis under certain conditions affecting a whole population may run an unusually violent course is shown in the case of endemic syphilis, especially as studied in Bosnia and Herzegovina. The following characteristics have been emphasized:⁵ frequency of extragenital infection acquired often during infancy and childhood, a tendency toward pustular, ulcerative, orbicular and follicular syphilids as second-

2. Neisser, A.: Beiträge zur Pathologie und Therapie der Syphilis, Julius Springer, Berlin, 1911, p. 202.

3. Von Düring: Erfahrungen in Kleinasien über endemische Syphilis, München. med. Wchnschr. **65**:1000 (Sept. 3) 1918.

4. Lambkin: An Outbreak of Syphilis in a Virgin Soil. Notes on Syphilis in the Uganda Protectorate, D'Arcy Power and Murphy: in A System of Syphilis **2**:337, 1914.

5. Glück: Zur Kenntnis der klinischen Eigentümlichkeiten der sogenannten endemischen Syphilis, Arch. f. Dermat. u. Syph. **72**:103, 1904.

ary manifestations, the appearance of precocious tertiary lesions, a high incidence of ulcerative destructive tertiary lesions and the comparative infrequency of visceral syphilis, especially tabes and paresis.

Syphilis of the negro in Africa has been the subject of a few reports, all lacking in detailed clinical or statistical study. In a survey of syphilis in the German colonies, Heim⁶ finds no differences between syphilis in the negro and in white people. Primary and secondary manifestations are generally disregarded by the natives. From the "Medical Reports for German East Africa" Heim makes the following statements: The initial lesion among the natives is persistent, but rarely phagedenic. Secondary manifestations are often severe with a tendency toward frequent recurrence. Glandular enlargement is often so extreme as to recall trypanosomiasis. In reviewing these reports over a period of seven years, Heim found only seven cases of tabes and two cases of general paresis recorded. He mentions Schroedter's observations of syphilis in German Southwest Africa, and states that roseola occurs in blacks, appearing as an intensification of the normal color of the skin. The dominating form of the secondary lesion in both male and female is the condyloma. Compared with syphilis in Germany, the course in the native is mild, even among tribes recently infected, no case of malignant syphilis, tabes or paresis being encountered.

Lambkin's⁴ report on syphilis in Uganda is of interest. About twelve years before his investigation, there had been a sudden outbreak of the disease among the Bagand tribe, and since that time it had increased in frequency and virulence until more than half the population was infected. Lambkin ascribes the rapid spread of the disease to the introduction of Christianity, resulting in abandonment of restriction on the liberty of women; to the abolition of punishment for all immoral offenses; and to the practice of vaccinating normal children with syphilis. The course was that usually described when syphilis is implanted on fresh soil and allowed to run riot. The initial lesion usually assumed the form of a Hunterian chancre and often became phagedenic. Secondary lesions were characterized by intense and confluent eruptions, ulcerations of the mucous membranes, laryngitis, iritis, periostitis and joint affections. Tertiarism manifested itself by early rupial syphilids, osteo-arthritic involvement with severe nocturnal pains, periostitis and osteomyelitis. Tabes and paresis were not common, possibly, in his opinion, because of the recent appearance of the disease. He had, however, observed a number of cases showing early tabetic changes.

6. Heim, Gustav: Die Syphilis in den deutschen Schutzgebieten, Arch. f. Dermat. u. Syph. **118**:165, 1914.

Baetz,⁷ in an analysis of 500 syphilitic negroes in a Canal Zone hospital, states that pain and disfigurement brought most of the patients to the hospital. Among 45 secondary cases presenting rashes, there were 19 papular, 14 papulo-pustular, 4 pustular, 4 maculo-papular and 2 macular eruptions. Mucous membrane lesions were not nearly so common as in whites. Vascular syphilis was frequent, including 10 cases of aortitis, 25 of aortic regurgitation and 15 of aneurysm. In the 366 patients who applied for treatment solely because of syphilis, pain, especially with nocturnal exacerbation, was the chief complaint in 277. He states that involvement of the osseous system in the tropical negro is in excess of that which occurs in the Caucasian in or out of tropical latitudes. Cerebrospinal syphilis occurred in 182 patients, in 51 with signs of cerebral hemorrhage or softening and in 12 with cranial nerve palsies. However, among the 20,000 admissions, not a single case of tabes was recorded, and only one case of paresis in a Columbian negro of Indian type.

References to syphilis in the negro of the United States are numerous, and subsequent mention will be made of these. Especially valuable are the investigations of Hazen, Fox, and Thompson, whose clinical and statistical studies are limited chiefly to dermatologic manifestations.

The material for this paper was obtained from the syphilis department of the Johns Hopkins Dispensary, a charitable clinic treating approximately 60 per cent. colored and 40 per cent. white patients. It should be stated that many of the negroes possess an admixture of white blood, and that this may modify results to a certain extent. No attempt was made to arrive at conclusions as to the relative frequency of syphilis in the two races. In all 1,843 cases were studied, distributed according to race and sex as follows: 596 white males, 521 colored males, 297 white females and 429 colored females.

AGE AT THE TIME OF INFECTION

Only cases of primary and secondary syphilis were used for comparing the age at the time of infection in the two races, as the majority of white and almost all black patients of the dispensary class either cannot definitely recall the date of infection or give a history of a series of genital sores, from which it is impossible to differentiate the primary lesion. The maximum number of infections occurs in white males and females during the twenty-second and nineteenth years, respectively; among the black males and females, in the twenty-first and seventeenth years, respectively.

7. Baetz: Syphilis in Colored Canal Laborers. A Résumé of Five Hundred Consecutive Medical Cases, *New York M. J.* **100**:820 (Oct. 24) 1914.

Table 1 shows that in negroes a much greater number of infections occur before the twentieth year than in white people. That over 50 per cent. of colored female syphilitics have been infected before the twenty-first year is due chiefly to their early indulgence in promiscuous sexual intercourse, the greater frequency of syphilis in that race, and the failure of the colored male with primary and secondary lesions to abstain from promiscuous intercourse.

TABLE 1.—AGE AT TIME OF INFECTION ACCORDING TO RACE AND SEX

Age	White Males		White Females		Colored Males		Colored Females	
	Num- ber	Per Cent.	Num- ber	Per Cent.	Num- ber	Per Cent.	Num- ber	Per Cent.
12-15.....	1		2		1		5	
16-20.....	32	13.6	25	35.6	51	23.9	67	53.7
21-25.....	89	36.7	24	31.6	88	40.6	41	30.6
26-30.....	49	20.2	19	25.0	41	18.9	17	12.7
31-35.....	38	15.7	4	5.3	25	11.5	2	1.5
36-40.....	19	7.8	2	2.7	6	2.7	2	1.5
41-50.....	14	5.8	0	3	1.9	0

Fournier,⁸ in analyzing 11,000 cases of syphilis in his private practice, found the maximum number of infections during the twenty-third year in males and during the twentieth year in females. However, that such figures do not correspond to those obtained from a charity clinic is shown by the statistics of Edmond Fournier⁹ from the Lourcine and St. Lazare Hospitals, patronized chiefly by prostitutes, in which the maximum number of infections occurred during the eighteenth year.

PRIMARY SYPHILIS

No differences were noted in the character of the chancre. Although Morrison¹⁰ states that induration of the chancre is more pronounced in the negro, no such difference was noted in the series here presented. Of twenty-seven extragenital chancres, only five occurred in colored patients. Of these three were labial, one was lingual, and one was on the abdomen. Thus the incidence of extragenital infection among white patients was 6.6 per cent. in contrast to 1.4 per cent. among colored patients. This observation agrees with statements of Hazen¹¹ and Thompson¹² that extragenital chancres are rare among negroes. Hazen, in a large experience with syphilis in the negro, encountered only one

8. Fournier, Alfred: *The Prophylaxis of Syphilis*, New York, 1906, p. 152.

9. Fournier, Alfred: *The Prophylaxis of Syphilis*, New York, 1906, p. 153.

10. Morrison, R. B.: *Personal Observations on Skin Diseases in the Negro*, Trans. Am. Dermat. Assn. (Sept. 18) 1888, p. 29.

11. Hazen, H. H.: *Syphilis in the American Negro*, J. A. M. A. **63**:463 (Aug. 8) 1914.

12. Thompson, L. B.: *Syphilis: Diagnosis and Treatment*, Philadelphia, Lea and Febiger, 1920, p. 52.

labial chancre. Illustrating the infrequency of extragenital infection in the colored race, Zeisler¹³ reported a case of multiple chancres of the lip in a negress. As an explanation for this relative freedom from extragenital infection, Reasoner¹⁴ suggests that there exists in the negro as in the rabbit a tissue defense against syphilitic initial infection outside of the genitalia.

EARLY SECONDARY SYPHILIS

This group comprises 507 patients; 152 white males, 76 white females, 147 colored males and 132 colored females.

Polyadenitis.—Glandular reaction in general is more marked in the negro, frequently to such an extent that cervicals, epitrochlears, even pectorals and preauriculars are visibly enlarged.

Pain.—Arthralgis, myalgia, periosteal and osteocopic pain were severe enough in twenty-four of the colored males and seven of the colored females to be included in the complaint, while only seven white patients were severely affected by such symptoms. Not infrequently in early secondary syphilis the negro presents symptoms of an intense reaction on the part of the bones and joints, namely, pain with severe nocturnal exacerbation, multiple circumscribed areas of exquisite periosteal tenderness, and at times, as occurred in three negroes in this series, marked effusion into the larger joints.

Iritis.—Only four, or 1.8 per cent. of the 228 white patients with early secondary syphilis presented an iritis. In 279 black patients there were thirty-six instances of acute iritis, or 12.9 per cent.; and it is noteworthy that seventeen of these were associated with follicular syphilids. Atkinson¹⁵ found eleven cases of iritis among 100 negroes with primary and secondary syphilis.

Mouth and Pharynx.—Secondary lesions of the buccal and pharyngeal mucous membranes exclusive of diffuse erythema were more common among white than among negro patients, occurring in 42.1 per cent. of the former and 27.2 per cent. of the latter. Hazen¹¹ states that mucous patches are more common in the negro. On the other hand, Baetz⁷ concludes that mucous membrane lesions are not nearly so common as in white patients. A singular observation is that of Carter,¹⁶

13. Zeisler: Multiple Chancres of the Lip in a Negress, J. A. M. A. **68**:1546 (May 26) 1917.

14. Reasoner, M. A.: Some Phases of Experimental Syphilis, J. A. M. A. **67**:1799, 1916.

15. Atkinson, I. E.: Early Syphilis in the Negro, Maryland M. J. **1**:135 (Aug.) 1877.

16. Carter, H. R.: Manifestations of Syphilis Among Negroes; A Statistical Inquiry, Rep. Superv. Surg.—Gen. Mar. Hosp., Wash. 131, 1883.

who did not observe a single mucous patch in 231 colored syphilitic patients, while such lesions occurred in twenty-one of a similar number of white patients.

Moist Papules and Condylomas.—Such lesions are much more frequent in the colored race, especially in the colored female. The incidence among white males and females was 11.8 and 26.3 per cent., respectively, among colored males and females 17.7 and 52.2 per cent., respectively. Hazen¹⁷ states that the fact that all syphilitic negro women suffer from condylomas at some time may help to explain the greater prevalence of syphilis in this race.

Syphilodermas.—Generalized eruptions occurred in 378 cases and were divided according to sex, race and type as shown in Table 2.

TABLE 2.—COMPARATIVE INCIDENCE OF SECONDARY SYPHILIDS IN WHITE AND NEGRO PATIENTS

	White Males		White Females		Colored Males		Colored Females		White Children per Cent.	Colored Children per Cent.
	Num-ber	Per Cent.	Num-ber	Per Cent.	Num-ber	Per Cent.	Num-ber	Per Cent.		
Macular.....	65	46.4	24	40.6	13	13.0	20	25.2	44.7	18.4
Maculopapular.....	40	28.6	18	30.4	14	14.0	16	20.2	29.1	16.7
Lenticular.....	19	13.6	9	15.2	13	13.0	12	15.1	14.0	14.0
Follicular papular....	10	7.1	4	6.8	30	30.0	19	24.1	7.0	27.3
Large flat papular....	1	0.7	0	3	3.0	0	0.5	1.7
Follicular pustular....	0	0	11	11.0	3	3.8	0.0	7.8
Large acuminate pus- tular.....	0	1	1.9	13	13.0	8	10.3	0.5	11.7
Rupia.....	5	3.6	3	5.6	3	3.0	1	1.3	4.0	2.7

Macular and maculopapular varieties comprised approximately 70 per cent. of the eruptions in white patients and 35 per cent. in the colored. The macular syphilid is unquestionably overlooked more often in the negro than in the white patient because of obvious difficulties attending its detection. According to Hazen,¹⁸ the macular syphilid comprises about 15 per cent. of early secondary rashes in negroes and over 50 per cent. in white people.

As noted by Stelwagon¹⁹ and Hazen,¹⁸ a striking peculiarity in the negro is the frequency of follicular lesions, both papular and pustular. Pustular syphilids, including both the follicular and the large acuminate pustular varieties, occurred in 24 per cent. of colored males and in 14.1 per cent. of black females, while in this series only one such pustular rash was observed among white patients. In a number of negroes, the eruption and associated fever and malaise aroused the

17. Hazen, H. H.: Syphilis, St. Louis, The C. V. Mosby Co., 1919, p. 115.

18. Hazen, H. H.: Syphilis, p. 90.

19. Stelwagon, H. W.: Diseases of the Skin, W. B. Saunders Co., 1914.

suspicion of variola. Only a relatively small number of cases of malignant syphilis were observed, and therefore no conclusions can be drawn as to their relative frequency.

Fox²⁰ characterizes as the most striking dermatologic peculiarity of the negro the annular papular syphilid, first described by Atkinson²¹ under the name of syphiloderma papulatum circinatum, and later emphasized by Gilchrist.²² In 1,000 consecutive cases in the dermatologic clinic of the Johns Hopkins Dispensary, among which there were seventy-two cases of syphilis in white and 193 in negro patients, Fox²⁰ encountered eleven such lesions in the negroes and none in the white patients; while Hazen,¹¹ in a series of 4,000 dermatologic cases, found forty-three annular papular syphilids in negroes and none in white patients. In the present series, among 228 white patients presenting manifestations of early secondary syphilis, typical examples of this lesion were encountered twice, while among 279 negroes it occurred in 40 cases.

Pruritus, unusual in white patients, is not infrequent in colored patients, especially in association with the follicular syphilid.

RECURRENT SECONDARY SYPHILIS

With the exception of condylomas, the cutaneous manifestations of recurrent secondary syphilis, which are often composed of a few insignificant lesions, seldom bring colored patients to the dispensary. Of sixty-eight white patients, only two suffered from recurrent pains, while among fifty-one negroes such symptoms were severe enough to return nine to the clinic. This tendency toward bone pain as a recurrent symptom accords with the relatively greater frequency of such complaints in early secondary syphilis.

TERTIARY SYPHILIS

The 887 cases in this group, inclusive of neurosyphilis, were distributed as follows: 269 white males, 152 white females, 248 colored males and 218 colored females. In Table 3 the various tertiary manifestations are divided according to structure involved, race and sex.

The negro is ignorant of the dangers of syphilis, and consequently is more apt to neglect treatment until the appearance of painful or destructive lesions. Numerous white patients visit the clinic to determine the status of a treated infection; on the other hand, the syphilitic

20. Fox, H.: *J. Cutan. Dis.* **26**:67, 1908.

21. Atkinson, I. E.: *Syphiloderma papulosum circinatum*, *J. Cutan. & Ven. Dis.* **1**:15 (Oct.) 1882.

22. Gilchrist, T. C.: Two Unusual Cases of Annular Syphilides in Negroes, *Maryland M. J.* **43**:1200, 1909.

negro is rarely asymptomatic at the time of his first visit unless sent from other departments of the hospital because of the accidental discovery of a positive Wassermann reaction. A colored syphilophile is a rarity.

TABLE 3.—COMPARATIVE INCIDENCE OF TERTIARY LESIONS OF SYPHILIS IN WHITE AND NEGRO PATIENTS

	White Males		White Females		Colored Males		Colored Females		White, per Cent.	Colored, per Cent.
	Num-ber	Per Cent.	Num-ber	Per Cent.	Num-ber	Per Cent.	Num-ber	Per Cent.		
Cutaneous.....	32	11.8	42	27.5	34	13.7	34	15.5	17.5	14.5
Gumma.....	11	4.0	19	12.4	31	12.4	21	9.6	7.1	11.1
Nodular.....	23	8.5	23	15.1	4	1.6	13	5.9	10.9	3.6
Bone.....	39	14.4	21	13.7	69	27.8	70	32.0	14.2	29.6
Nose and throat.....	32	11.8	19	12.4	39	15.7	42	19.2	12.1	17.3
Aortitis.....	32	11.8	9	5.9	52	20.9	18	8.2	9.7	14.9
Adenitis.....	3	1.1	3	1.9	6	2.4	17	7.7	1.4	4.9
Iritis.....	6	2.2	5	3.2	18	7.2	11	5.0	2.6	6.2
Elephantiasis.....
Vulvae and stricture of rectum.....	—	—	28	12.8	0.0	6.0
Orchitis.....	3	1.1	—	9	3.6	—	0.7	1.9
Neurosyphilis.....	155	57.6	36	23.6	71	28.6	28	12.8	45.3	21.0
Tabes.....	85	31.5	9	5.9	11	4.4	3	1.4	22.3	3.0
Paresis.....	15	5.5	4	2.6	4	1.6	4.5	0.8
Cerebrospinal.....	55	20.5	23	15.1	56	22.5	25	11.4	18.5	17.3

Cutaneous Manifestations.—Tertiary syphilids occurred in 17.5 per cent. of the white and 14.5 per cent. of the colored patients. Table 3 shows that the most common cutaneous lesion among white patients is the nodular syphilid, while among negroes it is the gumma. Of seventy-four white patients forty-six, or 62.2 per cent., presented nodular syphilids; of sixty-eight colored, only seventeen or 24.7 per cent. were of this type. Hazen,¹¹ in a series of 4,000 dermatologic cases equally divided between white and colored patients, reports gummatous lesions as occurring eighty times in negroes as compared with fourteen times in white patients, and nodular lesions nineteen times in negroes and 20 times in the white patients. That these two types of syphilids do not represent merely differences in localization of the same process in the cutaneous tissues, but rather a fundamentally different biologic reaction, is indicated by the experiments of Finger and Landsteiner.²³ Two patients with nodular syphilis when inoculated with material rich in *Spirochaeta pallida* developed corymbose lesions without ulceration, while thirteen patients with gummatous processes subjected to the same procedure developed ulcero-crustaceous lesions.

Osseous System.—The frequency of osteo-arthritic symptoms in early secondary syphilis in the negro would indicate a liability toward subsequent involvement of these structures. In fact, osseous lesions

23. Finger, E.: Die allgemeine Pathologie der Syphilis Handbuch der Geschlechtskrankheiten 2:944, 1912.

are about twice as frequent in colored as in white patients. Among white patients neurosyphilis exceeds bone syphilis in frequency, while in negroes the latter is the most common form of tertiary syphilis.

Vascular Syphilis.—Osler²⁴ states that in the wards for colored patients at the Johns Hopkins Hospital, syphilitic arterial disease and aneurysm were relatively more common than in the wards for white patients. Of 345 aneurysms, 213 occurred in white and 132 in negro patients, while the proportion of admissions of white to negro patients was about 5 to 1. In an analysis of 2,376 admissions to the medical service of the same institution, Janeway²⁵ found a positive Wassermann reaction in 37.6 per cent. of the 347 colored and 8.8 per cent. of the 2,029 white patients. Among the latter there were thirty-one cases of aortic syphilis and among the former fifty cases, a comparative incidence of 10 to 1. He suggests that the syphilitic negro, since he engages in manual labor to a greater extent, is more liable to develop aortic syphilis and especially aneurysm than the white patient. As shown in Table 3, about 15 per cent. of the black and 10 per cent. of the white patients presented signs of aortitis; in males alone of the two races, the ratio was approximately 2 to 1, with the blacks predominating. Aneurysm occurred in fourteen negroes and in six white patients. In interpreting Janeway's statement that aortic syphilis is ten times more frequent in negroes than in white patients, it must be taken into consideration that his conclusions are based on a series of patients including nonsyphilitics, and that he does not take into account the fact that syphilis, as manifested by a routine Wassermann reaction was four times more frequent in the colored race. When a racial comparison is made from his statistics based on syphilitic cases only, it is seen that aortitis was diagnosed in 38 per cent. of the colored and in 17 per cent. of the white syphilitics, a ratio approximating that obtained in the present series.

Adenitis.—In this group are included only those cases in which the diagnosis was confirmed by a therapeutic test. It is striking that of twenty-nine cases of tertiary adenitis, twenty-three occurred in negroes. All but one of twelve cases of lymph-gland gummas observed by Hazen²⁶ were in black patients. There is a more marked reaction on the part of the lymph glands in early secondary syphilis in this race, and a correspondingly greater tendency toward gummatous adenitis in the subsequent course of the disease.

24. Osler, W.: *Modern Medicine*, Philadelphia, Lea and Febiger 4:452, 1908.

25. Janeway, T.: *The Etiology of Diseases of the Circulatory System*, Boston M. & S. J. 174:925, 1916.

26. Hazen, H. H.: *Syphilis*, p. 232.

Iritis.—As in early secondary syphilis, the negro is especially prone to develop iritis as a late manifestation. Of forty cases in which this occurred as an isolated lesion or in association with other tertiary lesions, twenty-nine were colored patients.

Leukoplakia.—Leukoplakia occurred in eight white males, one white female, and in two colored males. In one of the latter it was associated with carcinoma of the tongue. That this condition is relatively rare in the negro is evidenced by statistics compiled by Fox²⁰ from the statistics of dermatologists with a large experience among this race.

Elephantiasis Vulvae and Stricture of the Rectum.—This group undoubtedly includes nonsyphilitic lesions. Jersild,²⁷ in a recent article in which he emphasizes the fact that some lesions of this type are not syphilitic, reports cases in which the original diagnosis of syphilis was shown to be erroneous by the subsequent development of primary and secondary syphilis. Jones²⁸ observed forty-eight cases of stricture of the rectum, forty-seven in black females and one in a black male. He states that forty-six of these cases were undoubtedly syphilitic. In ten cases of stricture of the rectum in colored patients, McNeill²⁹ found a positive Wassermann reaction in all but one. In my series, elephantiasis vulvae occurred in twelve negroes, stricture of the rectum in nine, and a combination of the two conditions in two. It is striking that not a single white woman presented such lesions.

Neurosyphilis.—Neurosyphilis, occurring in 45.3 per cent. of the white patients (Table 3), is the most common form of late syphilis in this race.

In 4,400 cases of tertiary syphilis observed by Fournier³⁰ in his private practice (almost exclusively white patients), 1,857 or 42 per cent. presented neurosyphilis. He states that the nervous system bears the brunt of tertiarism with a frequency which he was far from suspecting until he compiled his observations. In the present series neurosyphilis occurred in only 21 per cent. of the cases of late syphilis among negroes, being surpassed by tertiary lesions of the bones with 29.6 per cent. That the negro is less liable to develop neurosyphilis is supported by an analysis of routine spinal fluid examinations in treated syphilis by Moore³¹ of this clinic. In 377 white patients the spinal fluid showed changes in 60 or 15.9 per cent. of the cases. In 265 negroes only 22 or 8.3 per cent. of the spinal fluids were pathologic.

27. Jersild, O.: Contribution à l'étude de la pathogénie du soi-disant syphilome ano-rectal, *Ann. de derm. et syph.* **1**:62, 1920.

28. Jones: Syphilis in the Negro, *J. A. M. A.* **42**:32, 1904.

29. McNeill: Syphilis in the Southern Negro, *J. A. M. A.* **67**:1001, 1916.

30. Fournier, A.: *The Prophylaxis of Syphilis*, New York, 1906, p. 140.

31. Moore, J. E.: The Cerebrospinal Fluid in Treated Syphilis, *J. A. M. A.* **76**:769 (March 19) 1921.

A comparison of the various types of neurosyphilis shows striking racial differences. Cerebrospinal syphilis, including both the meningitic and endarteritic forms, was approximately of equal frequency in the two races. Basilar meningitis with its cranial nerve disturbances and cortical meningitis with its epileptiform attacks, were as common among the negroes as among white people. A noteworthy characteristic of cerebrospinal syphilis in black patients appears in its greater liability to assume the endarteritic form. Symptomatic cerebral endarteritis was observed in twenty negroes, and in only nine white patients. Examination of a random number of cases, about equally divided between the two races, in the Municipal Hospital records showed twenty-four such cases among negroes and eight among white patients.

In contrast to the meningitic and endarteritic types of cerebrospinal syphilis, tabes is relatively rare in the negro. In the survey at the Municipal Hospital referred to there were twenty-four white and only two colored tabetic patients. In my series tabes was diagnosed in ninety-four white and in fourteen colored patients.

In 1882, Burr³² called attention to the infrequency of tabes in the colored race. More recently Hecht,³³ in reporting the cases of four colored tabetics with advanced optic atrophy, suggested that tabes probably exists in the colored race more commonly than has been supposed, and that failure to recognize it is due to the abeyance or total absence of ataxic symptoms in the amaurotic type. He also suggests that admixture of white blood has made the negro more liable to tabes. In a statistical study of 250 cases of tabes in the Philadelphia General Hospital, Lucke³⁴ reports thirteen cases in colored males and one in a colored female. The relative number of white and colored patients treated at the hospital is not, however, given. According to Maloney,³⁵ tabes is rare in races which are not exposed to the turmoil of civilization. The negro, in whom the occurrence of tabes at one time was the exception, yearly enters more and more into the competition of modern life and is losing his freedom from this form of syphilis.

Paresis.—That there were only twenty-four parietic patients in this series is explained by the fact that patients with definite mental symptoms are referred for the most part to the psychiatric clinic. There were twenty white and four colored patients, suggesting a comparatively high ratio of paresis in the white race.

32. Burr: The Frequency of Locomotor Ataxia in Negroes, *J. Nerv. & Ment. Dis.* **17**:278, 1892.

33. Hecht; Tabes in the Negro, *Am. J. Med. Sc.* **126**:705, 1903.

34. Lucke: Tabes Dorsalis, A Pathological and Clinical Study of Two Hundred and Fifty Cases, *J. Nerv. & Ment. Dis.* **43**:393, 1916.

35. Maloney: Locomotor Ataxia, New York, Appleton and Co., 1918, p. 147.

Combined Lesions of Aortitis and Neurosyphilis.—In twenty-two white patients, aortitis was associated with neurosyphilis. Of these, sixteen were tabetic and three showed changes resulting from cerebral endarteritis. On the other hand, such a combination was diagnosed in nineteen negroes, of whom three were tabetic and twelve had cases of cerebrospinal syphilis with endarteritic lesions. Accordingly, aortitis in the negro was most frequently associated with cerebrospinal syphilis of the endarteritic type, while in the white patients it was most frequently associated with tabes.

Congenital Syphilis.—Only late forms of congenital syphilis are treated in the syphilis clinic. There were twenty-seven white males, thirty-four white females, fourteen colored males and twenty-eight colored females with symptoms of syphilis hereditaria tarda. No noteworthy difference was found in the two races.

Interstitial keratitis occurred in nine or 33.3 per cent. of the white males, in twenty-one or 61.7 per cent. of the white females, in five or 35.7 per cent. of the colored males, and in twenty-one or 75.0 per cent. of the colored females. Such a predominance of keratitis in the female has been noted frequently. In Igersheimer's³⁶ series of the 257 patients with syphilitic keratitis, there were 127 males and 130 females. In his analysis of these groups, he found that the males represented 40 per cent. of all cases before the twentieth year, and 62.9 per cent. of those over 20 years.

SUMMARY

Primary Syphilis.—Extragenital infection is relatively infrequent in negroes. Among colored males and females, the age of infection is respectively one and two years earlier than in white males and females.

Secondary Syphilis.—Secondary syphilis in the negro is characterized by marked polyadenitis, by frequent and severe osteo-arthritic symptoms, by the frequency of iritis, and by the high incidence of follicular and pustular syphilids. A striking racial peculiarity is the frequent occurrence of the annular papular syphiloderm.

Tertiary Syphilis.—Bone syphilis is the most frequent lesion of tertiary syphilis in the negro, exceeding neurosyphilis, which in white patients comprised almost half of all late manifestations.

Cardiovascular syphilis is more frequent in the negro, with an incidence of two to one in colored and white males, respectively.

Stricture of the rectum and elephantiasis vulvae are extremely common in the colored female.

Leukoplakia is rare in the negro.

Tertiary adenitis is common in the negro.

36. Igersheimer: Syphilis und Auge, Julius Springer, Berlin, 1918, p. 217.

Neurosyphilis is more frequent in white patients than in negroes. The negro is less likely to develop tabes or paresis, while the large group of unclassified cases of cerebrospinal syphilis is approximately of equal frequency in the two races. In negroes it is especially likely to manifest itself in the form of cerebral endarteritis.

CONCLUSION

In respect to syphilitic infection there exist inherited biologic differences between white and negro patients. The negro develops intense reactions on the part of cutaneous and osseous structures, and is relatively free from tabes and paresis. In white patients, syphilis more frequently runs its course with skin manifestations slight or absent, but there is a greater tendency toward the eventual development of tabes or paresis.

Abstracts from Current Literature

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XVI. THE INFLUENCE OF TEMPERATURE AND DURATION OF PRIMARY INCUBATION ON THE VELOCITY AND AMOUNT OF COMPLEMENT FIXATION IN SYPHILIS WITH DIFFERENT ORGAN EXTRACTS (ANTIGENS). JOHN A. KOLMER, ANNA M. RULE and ELIZABETH M. YAGLE, *Am. J. Syphilis* **5**:44 (Jan.) 1921.

The authors conclude:

1. Complement fixation with strongly syphilitic serums is frequently rapid and may occur immediately at room temperature and especially with cholesterolized and acetone-insoluble lipoid extracts as antigens; incubation at 38 C., however, usually increases the amount of complement fixation.

2. Complement fixation in syphilis is usually, but not always, more complete in an open water-bath at 38 C. than in an air incubator at the same temperature; one-half hour in a water-bath, however, is not usually equal to one hour in an incubator, as is commonly stated.

3. The velocity and amount or degree of complement fixation at 38 C. varies greatly according to the organ extract used as antigen, being more rapid with cholesterolized extracts and least with plain or crude extracts.

4. In general terms, complement fixation in syphilis reaches the maximum degree at 38 C. in a water-bath with extracts of acetone-insoluble lipoids in from thirty to forty-five minutes; with cholesterolized extracts in from one to two hours, and with plain or crude alcoholic extracts at least two or three hours are required.

5. Primary incubation at 20 C. (room temperature) results in less complement fixation than in a water-bath at 38 C. for one-half hour; two hours at 20 C. results in a fixation of complement about equal to one hour at 38 C.

6. Complement fixation in syphilis at from 0 to 8 C. is frequently rapid, well marked reaction being observed even after incubations of only fifteen minutes.

7. At temperatures of from 8 to 10 C. complement fixation in syphilis occurs more slowly than at 38 C., but the degree or amount of complement fixation is greater; this is especially true with plain or crude extracts.

8. Complement fixation in syphilis occurs somewhat more rapidly at 8 C. than at from 0 to 2 C.; the optimum temperature for cold incubation is from 6 to 15 C. and the optimum time from four to eighteen hours.

9. At 38 C. for from one-half to two hours complement fixation in syphilis is much more rapid and greater in degree with cholesterolized and acetone-insoluble extracts as antigens than with plain or crude extracts; at from 8 to 10 C. for about eighteen hours the difference in degree of complement fixation among the different extracts is not so marked, although the reactions with cholesterolized extracts are usually slightly stronger than with plain extracts.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XVII. A COMPARATIVE STUDY OF METHODS FOR CONDUCTING THE PRIMARY INCUBATION FOR COMPLEMENT FIXATION IN SYPHILIS WITH THE TECHNIC RECOMMENDED FOR A STANDARDIZED TEST. JOHN A. KOLMER, TOITSU MATSUNAMI and MARY E. TRIST, *Am. J. Syphilis* **5**:63 (Jan.) 1921.

The authors conclude:

1. In comparative complement-fixation tests in syphilis, employing the same technic but with one primary incubation in a water-bath at 38 C. for one hour and a second in a refrigerator at 8 C. for from four to eighteen hours, there was no evidence of the existence of one antibody-fixing complement best at 38 C. and a second reacting best at 8 C. The only difference encountered were positive reactions with some serums tested at 8 C. which reacted negatively at 38 C. and stronger reactions with some serums at 8 C. than at 38 C., especially with plain antigens. No syphilitic serums have been encountered yielding positive complement-fixation reactions with a primary incubation of one hour at 38 C. and negative reactions at 8 C. for from four to eighteen hours, provided the same antigen was employed in both.

2. Primary incubation at from 8 to 10 C. for from four to eighteen hours results in greater fixation or absorption of complement by serums and antigens alone than that occurring during one hour at 38 C., but also results in the specific fixation of more complement by mixtures of serum and antigen. Complement fixation is slower but more complete at 8 C. than at 38 C., especially with plain antigens.

3. Comparative studies in complement fixation in syphilis with two quantitative methods, three different antigens and seventeen different kinds of primary incubation, have shown that the best methods for conducting the primary incubation from the standpoint of sensitiveness of the reactions, are (a) three or four hours at from 8 to 10 C. plus one hour in a water-bath at 38 C., and (b) eighteen hours at 8 to 10 C. in a refrigerator. With either of these methods, however, the kind and amount of antigen employed and adjustment of the hemolytic system are factors of much importance in order to avoid nonspecific reactions.

TOMLINSON, Omaha.

EDEMA IN MAN. F. SAMBERGER, *Ceska dermat.* **1**:3, 1920.

The pathogenesis of edema is as yet an unsolved problem. From dermatologic experience we know two types of edema. They differ both clinically and pathologically and have also a different pathogenesis. They are: 1. Lymphatic edema, which results from abnormal accumulation of lymph and tissue fluids in a certain locality either (a) by hyperproduction of lymph or (b) by retention of lymph. The lymph is secreted by the endothelium of blood capillaries. It is an active process controlled by special nerves and responding to direct and reflex stimuli. The production of lymph can be, therefore, actively increased. Resulting edema comes on suddenly, and disappears suddenly with removal of the cause. Under this classification of edema belong: acute edema of Quincke, the urticarial wheal, and the bulla of pemphigus. Just how the lymph returns from the tissues is not definitely settled. The author believes that, under normal conditions, the lymph returns from the tissues only by means of its own channels (as illustrated by the fact that total extirpation of inguinal lymph glands is followed by elephantiasis of the corresponding area).

Therefore, whatever will block the lymph channels will prevent the outflow of lymph from the part. Resulting swelling is a passive lymph edema. It comes on gradually, and remains stationary if the interference with outflow is permanent. The edema is solid; the skin of the affected area is yellowish, but not anemic.

2. Serous edema, which is best known in connection with nephritis and decompensated heart diseases. The skin never hypertrophies, even if edema should last for months. The fluid of serous edema must be different in its composition and genesis from that of lymph, with its nutritive qualities. The study of genesis of edema in these cases is difficult on account of the complicated nature of their pathologic processes. The author had an opportunity to study a simple case of serous symmetrical edema of the face in a young soldier. The patient was exposed to bitter cold in the field. His face was frost bitten. In twenty-four hours the entire face became considerably swollen. He improved slightly in the hospital. In summer, edema became barely noticeable, but it returned in winter. Physical examination of the soldier was entirely negative otherwise. It was a case of so-called "white edema," known among soldiers since Charles VI, and of simple pathogenesis. Cold affects the vitality of blood capillaries in the skin. They no longer carry blood as normally. The serum, and in the most severe cases also the formed elements, pass through damaged capillary walls and saturate the tissues. The normal production of tissue fluids, however, stops, and the cells soon show undernourishment. The skin becomes thin, transparent, pale and cold. The case illustrates the fact that serous edema is caused by weakened activity of diseased blood capillaries.

The author further calls attention to the "purplish-red edema" occurring in anemic persons in cold weather, and limited to fingers and hands. It is a case of passive congestion and edema, cold affecting only the venous element of capillaries (acro-asphyxia) while the arterial side is functioning properly.

Inflammatory edema is a serous edema, and accompanies all cases of inflammation. In some cases edema takes place in surrounding tissues, without other pathology. If the offending organism is very virulent, capillaries of a wide area become paralyzed, and an extensive edema takes place. The weaker the host, the less the vitality of the capillaries, the easier it is for such edema to develop.

Malignant edema, comparatively common in war times, is an extreme example.

CEPELKA, Chicago.

LIQUORBEFUNDE BEI BEHANDELETER SYPHILIS (SPINAL FLUID FINDINGS IN TREATED SYPHILIS). THEODOR KOHRS, Dermat. Ztschr. 22:71, 1921.

Kohrs, having reported last year on the spinal fluid of untreated syphilis, sought to learn the findings in the fluid of treated patients. He wished to learn, if possible, the differences between the two, what factors operated, and the connection of both to the problem of paresis and tabes.

Among the conclusions arrived at are: Changes in the fluid, that are evident in the primary stage of syphilis, are brought back to normal by ordinary intravenous therapy. If the changes occur in the secondary stage and are manifest clinically, it is possible by intravenous treatment to alter the pathologic findings—in the majority of cases to normal. On the other hand, if a

course of treatment, for example with arsphenamin, is interrupted after the injection of 0.9-1.5 gm. a number of such patients are certain to have worse meningeal symptoms.

Among the patients with so-called recidive lesions of the skin or mucous membranes, at least 75 per cent. showed grave changes in the spinal fluid. One must remember that in the untreated syphilitic patients there may be early meningeal changes, which with insufficient treatment may be healed. Treatment in the later years after infection are less likely to give favorable results.

The percentage is about the same for alterations in the spinal fluid of the treated and untreated cases. No one reaction of those used in the laboratory seems to be more prevalent among the two groups as a mark of distinction. The albumin was increased in most cases of latent syphilis.

The author has the impression that early meningeal involvement may be successfully treated with energetic intravenous therapy. The idea that meningeal symptoms are more frequent following the use of arsphenamin symptomatically is not borne out in his experience. Rather, it has appeared that the meningeal recidive is more frequent among those treated with a full course of arsphenamin, against the so-called symptomatic use of the drug.

Intravenous treatment has seemed to give favorable results in known cases of gummatous disease of the central nervous system and in cerebrospinal syphilis. Gennerich is credited with this observation also.

The few intraspinal cases in the personal experience of the author have not seemed to give the results expected, and though the immediate results may have been better, later observations on the spinal fluid did not show any better results than were obtained with the fluid of patients treated by the intravenous method alone.

Two of the patients were treated with injections of arsphenamin into the carotid. The results were such as to influence the author to try this method further.

The war has made it difficult for the author to follow his cases in order to learn the clinical status of those punctured. It would appear, however, from the results obtained that the patients who developed paresis or tabes were not necessarily those that had shown evidence of early meningeal involvement.

GOODMAN, New York.

COMBINATION ABORTIVE TREATMENT OF SYPHILIS. HUGO HECHT, Arch. f. Dermat. u. Syph. **126**:327, 1918.

The first observations concerning the rapid disappearance of manifestations of syphilis following the injection of single doses of arsphenamin caused the belief that the "sterilisatio magna" dream of Ehrlich had been realized. Further studies, however, seemed to prove that arsphenamin alone was not sufficient, and that the combination of mercury and arsphenamin gave better and more permanent results. Various methods of using the two have been advanced, and Hecht had the opportunity to study cases of abortive treatment results over a period of nine months, which he considers the minimum, and others which were not observed that long, and hence not included in his summary and conclusions.

Abortive treatment of syphilis should be begun after a positive diagnosis has been made by the demonstration of *Spirochaeta pallida*. The primary lesion should be excised or destroyed. At all events, the primary lesion or its scar should be kept covered with mercurial plaster. Treatment should consist of three or four arsphenamin or from four to six neo-arsphenamin injections,

and fifteen calomel injections. According to the personal requirements of the individual case, these injections may be increased or diminished. Patients with negative Wassermann reactions at the beginning of the course should have the test repeated every week, as any sign of a positive blood reaction indicates more intensive treatment. If the Wassermann reaction is positive at the onset of treatment, protracted mercury courses are to be given. Treatment should certainly be continued until the serology is negative. The final Wassermann reaction should be controlled by one of its more delicate modifications (Hecht or Stern). If the negative reaction is not secured by the outlined treatment it should be repeated after a rest of one month. Complete physical and serologic examinations should be repeated at four month intervals for the first two years. At the close of the first nine months following infection, the serology should be studied after an injection of arsphenamin (provocative), and the cerebrospinal fluid should also be examined.

The greater proportion of recurrent lesions (recidive) occur during the first nine months. After that such recurrences are rare. Most of them would be the result of insufficient or uncompleted courses of treatment. Insufficient arsphenamin predisposes to neurorecidive lesions.

If a patient remains Wassermann negative and symptom free for nine months, he is in all probability permanently cured. The positive Wassermann reaction in latent syphilis is a sign of syphilis and indicates further treatment.

Five years of observation affords Hecht the opportunity to conclude that abortive cures are possible within certain limits in syphilis. The negative Wassermann reaction on the serum and negative findings in the spinal fluid increases the possibility that the conclusion based on clinical observations is correct. Further proof is afforded by numerous cases of reinfection.

Hecht gives these requirements for reinfections:

1. Positive proof of the existence of first chancre by demonstration of spirochetes.
2. Thorough treatment.
3. One year of freedom from symptoms with repeated negative clinical and serologic examinations.
4. Negative Wassermann reactions even after provocative injection of arsphenamin nine months after the close of treatment, and use of delicate modifications of the Wassermann test.
5. Second infection proved by normal incubation time, demonstration of spirochetes and typical appearance of the lesion.
6. Negative Wassermann reaction at the beginning, which on repeated tests becomes positive.
7. Gradual enlargement of the draining lymph nodes, first unilateral, then bilateral.
8. Appearance of a typical first exanthem with no treatment of the patient.

Müller demands two further considerations which Hecht regards as unnecessary, namely, that the Wassermann reaction should be entirely negative during the first infection, and that the second chancre should not be in the same draining lymph areas. Acceptance of the first consideration, according to Hecht, means that the possibility of curing syphilitic patients when the Wassermann reaction is positive, is denied.

Hecht closes this paper of over fifty pages with a lengthy bibliography (which he says is incomplete) of over 150 titles.

GOODMAN, New York.

DOSAGE MEASUREMENT. A CRITICISM. J. S. SHEARER, *Am. J. Roentgenol.* **8**:145, 1921.

Shearer does not question either the therapy, care or skill in reading pastilles by Remer and Witherbee, and he disclaims any effort on his part to discuss dosage in therapy. Still he wishes to call attention to the fact that what therapists will do with radiation depends very much on their conception of the physical side. The extension to higher or lower voltages, and the choice of filters ought to be based on the correct use of the physics involved, to the end that therapists may secure reproduction of results and may be sure that the differences are due to the patient, and not to the radiation utilized.

It seems to Shearer quite unfortunate at this time, when we are shortly to be able to clear up many of the disputed points in therapy, to have several articles appear giving quite erroneous interpretations of observations.

The first article of Remer and Witherbee in June, 1917, questioned the voltage law as measured by pastilles. In the same article the inverse square law was questioned when filters were used. When writers challenge the validity of well established physical laws, they must expect a critical scrutiny of their contentions. So in the present case, various statements of these authors must be considered as to their concordance and probability.

Shearer compares statements made in an article by Remer and Witherbee published in the *New York Medical Journal*, June 26, 1920, to those of earlier communications from these authors. It appears that several contradictions, reversals of opinion and real errors have crept into their work. Shearer says that in the June, 1920, paper, Remer and Witherbee admit the inverse square law is right for unfiltered rays, which was denied in 1917.

It seems significant to Shearer also that the pastille readings are not in accord with the prediction of physical laws in regard to the fact that dosage is proportionate to time. In another place, Shearer analyzes the law of uniform increase of dose with time, and asserts that Remer and Witherbee used Holz-knecht and Kienbock scales which are fixed by the very laws whose validity they deny.

Shearer also plotted as a curve Remer and Witherbee's exposure times for 1 Holz-knecht unit, current, distance and gap constant, but using different thicknesses of aluminum. The plot is an irregular line, which, according to Shearer, is highly improbable.

In the article "Cause of X-Ray Burns" (*Med. Rec.*, July 31, 1920), Shearer finds more cause for criticism, as also in the article in the *American Journal of Roentgenology*, October, 1920, which in fact in the main is a rearranged reprint of the others, according to Shearer.

GOODMAN, New York.

SOME FACTORS RELATING TO THE TOXIC ACTION OF ARS-PHENAMIN. R. HUNT, *J. A. M. A.* **76**:854 (March 26) 1921.

In his experimental studies the author has observed three distinct types of toxic action due to arsphenamin: (a) that caused by "arsenoxid"; (b) that due to the presence of toxic substances other than the oxid mentioned; and (c) that resulting from the physical properties of the solution or from the presence in it of an easily destroyed poisonous compound.

In so far as the presence of arsenoxid is concerned, no toxic commercial preparation of arsphenamin was encountered in which the toxicity appeared to be due to the presence of this substance. However, its formation is assured if sufficient aeration of an arsphenamin solution occurs. Warming and further aeration of such a toxic solution decreases the toxicity through further oxidation.

It is conceivable that extremely poisonous substances containing sulphur may be present in arsphenamin, as well as other sources of contamination which may creep in during the preparation of the drug; but these highly toxic compounds have not been isolated or identified.

Hunt has observed instances that lead him to believe that the physical condition of the solution may at times account for untoward reactions. This belief however, requires substantiation. The possibility of the presence, in some preparations of arsphenamin, of a toxic product easily hydrolyzed by alkali must be considered. This possibility further complicates the study of clinical reactions due to the drug. For instance, the warmth of the solution at the time that the alkali is added, as well as the length of time that the prepared solution stood before it was administered, might change either the chemical or the physical state of the solution. For example, it has happened that a number of patients received arsphenamin of the same lot by the same method of administration, and only one or two showed reactions. Idiosyncrasy has been invoked to explain these puzzling occurrences; whereas, according to the author, if the one or two showing the reactions were the first to receive the drug, the reactions may have been due to the physical condition of the solution, which spontaneously changed before the injections that were borne without reactions were made.

MICHAEL, Houston, Texas.

SPIROCHAETA PALLIDA IN THE MOUTH. P. SAVNIK, Ceska dermat. 1:169, 1920.

The great frequency of syphilitic lesions in the mouth led the author to a study of *Spirochaeta pallida* as regards the danger of contagion and the resistance to various chemicals.

The results of examinations were:

No. of Cases	Lesions	Spirochetes
25	Chancre	4
48	Syphilis (secondary)	34
6	Gumma	0
34	Syphilis (latent)	5
<hr/> 113		<hr/> 43

During treatment spirochetes disappeared in three patients with primary syphilis treated with mercury rubs, 3 gm. daily, one after five, one after ten, and one after fifteen rubs.

Secondary Stage: In eleven patients, treated with mercury rubs, after five days 1 was found negative and 10 positive; after 10 days, 3 were negative and 8 positive; after fifteen days, 6 were negative and 5 positive; after twenty-nine days, 9 were negative and 2 positive; after twenty-five days, 9 were negative and 2 positive.

In two cases, negative at the start, spirochetes were found in the course of treatment. Of three patients with specific angina treated with mercuric salicylate (1 gm. every fifth day), two became negative twenty-four hours after the third, and one after the fourth injection. Of four patients treated with neo-arsphenamin, two became negative twenty-four hours after the first injection. Nine patients with secondary syphilis receiving a combined treatment showed how much more effective neo-arsphenamin is than mercury in destroying the spirochetes. The smallest dose (0.3 gm.) is not sufficient.

The author further gives the result of the action of twenty different chemicals on the spirochetes under the microscope, and concludes that for practical purposes 4 per cent. boric acid solution seems the most satisfactory gargle. It is quite efficient in keeping the surface of the buccal mucosa free of spirochetes. Regular gargling can reduce the danger of accidental contagion.

CEPELKA, Chicago.

THE NATURE OF PSORIASIS. F. SAMBERGER, *Ceska dermat.* **2**: No. 6.

The author declares that psoriasis is a suppurative inflammation of the skin, caused by some irritant damaging the epidermal cells in a person with a parakeratotic diathesis. This diathesis is the main reason why typical psoriatic lesions appear instead of trivial suppurative lesions. Usually staphylococci and streptococci furnish the exciting cause, only occasionally other germs or chemical irritants.

Pathologically the changes appear as epidermal miliary abscesses under a parakeratotic horny layer. Exfoliation of cells leads to the opening of abscesses and the discharge of the content. The less the vitality of cells, the faster they separate. The scales are then thin and silvery. With increase in the vitality of cells they become more adherent; more pus can accumulate between the layers. The scales become thicker, yellowish, and look like pus crusts.

Realizing that the thymus had something to do with the vitality of the skin, the author was led to experiment with thymus hormone and arrived at the conclusion that parakeratotic dysfunction of the skin yields to thymus therapy. Brock arrived at similar conclusions. He considers thymus hormone as the causal therapy, however, while Samberger takes it only for symptomatic. According to him, thymus insufficiency is only one of the causes of parakeratotic dysfunction. Anything that will increase the vitality of epidermal cells will clear up psoriasis: arsenic, roentgen rays in stimulating doses, etc.

CEPELKA, Chicago.

CONTRIBUTION TO STUDY OF EXFOLIATIVE ERYTHRODERMAS FROM ETIOLOGIC POINT OF VIEW. J. SCHAUMANN, *Acta dermatoven.* **3-4**:389 (Dec.) 1920.

This author reports the observation of an exfoliating erythroderma which appeared in a case of Hodgkin's disease following a vaccinal lupus. The patient, a man of 64 years, had an old extensive lupus vulgaris on his right arm of vaccinal origin, which spread in spite of radiotherapy and phototherapy, so that it finally involved the trunk. After six years diarrhea developed, accompanied by loss of weight. A little later the skin became red and exfoliative, the entire body surface being thus affected; the pubic and axillary hair disappeared. Fever accompanied the process, and as it went on the lupus entirely subsided. At necropsy the lymphatic system showed a malignant lymphogranulomatosis, which is often confused with pseudoleukemia, but whose distinctive points have been shown by Sternberg. The diagnosis of Hodgkin's disease was made. This case argues in favor of a tuberculous etiology in the lymphatic infection.

An interesting résumé of the exfoliating erythrodermas is given, based on the question of etiology. Those probably associated with tuberculosis are considered; then malignant lymphogranuloma, benign lymphogranuloma, lepra, mycosis fungoides, pseudoleukemia and lymphatic leukemia (incidentally including the theory that the itching "leukemides" and some other urticarial eruptions

are due to the circulation of products of nuclear decomposition, from the excessive breaking-up of blood cells in the spleen and elsewhere); divers infections and intoxications (including drug intoxications); psoriasis, seborrheic eczema, lichen planus and erythema multiforme. The matter of differential diagnosis is then considered.

PARKHURST, New York.

IDIOSYNCRASY TOWARD ROENTGEN RAYS. DR. K. GAWALOWSKI, *Ceska dermat.* 1:24, 1920.

Injurious effects of roentgen rays manifest themselves most frequently as acute or chronic dermatitis; less often as alopecia, oligospermia or azoö spermia. The author reviews the three usually accepted degrees of roentgen dermatitis: (a) erythematos, (b) bullosa, (c) ulcerosa or gangrenosa, and adds the histologic findings. There are variations from normal response to rays, and cases of increased and decreased sensitiveness. By idiosyncrasy is meant a reaction of abnormal character or intensity to a given dose. The tendency to blame uncritically all untoward results of roentgen-ray therapy on idiosyncrasy soon met with opposition, and many authors went to the other extreme and denied the possibility of idiosyncrasy, explaining poor results by errors in dosage and imperfection of the methods used. The author cites five cases which tend to prove the existence of idiosyncrasy, and also recalls Bergonnié-Tribondeau's experimental work on mice. The meaning of so-called "early reaction" and "artificial reaction" are as yet unsettled. Most authors do not consider "an early reaction" as a manifestation of idiosyncrasy. They believe that it depends largely on the irritability of blood vessels (frequent in exophthalmic goiter).

Atypical reactions manifest themselves in two ways: (a) as an erythema or a papular exanthem on unexposed surfaces, and often accompanied by a rise of temperature; or (b) as eczematous dermatitis in the vicinity of the treated area. The latter is considered neuropathic in origin or due to the toxic effect of broken-down cells.

Sensitiveness to roentgen rays is increased physiologically during menstruation and pregnancy. Certain pathologic states are accompanied by increased sensitiveness: diabetes, arteriosclerosis, gout, cachectic states and certain injuries. It is therefore advisable to take them into consideration when deciding on dosage. Clinical and experimental work shows that an acutely hyperemic skin is very sensitive (acute lesions of psoriasis). Search through the literature shows few cases of decreased sensitiveness. German clinics report several instances of absolute overdose without even an erythema. From the legal standpoint it is advisable to follow rather closely one of the well-recognized dosage systems, which afford the best protection against possible untoward consequences of exposures.

CEPELKA, Chicago.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XV. THE INFLUENCE OF TEMPERATURE AND DURATION OF PRIMARY INCUBATION ON THE ANTICOMPLEMENTARY ACTIVITY OF ORGAN EXTRACTS (ANTIGENS) AND SERA. JOHN A. KOLMER and MARY E. TRIST, *Am. J. Syphilis* 5:30 (Jan.) 1921.

The authors conclude:

1. Temperatures of 37 to 38 C. particularly increase the nonspecific fixation or inactivation of complement by organ extracts or antigens and serums commonly designated as the anticomplementary activity of these substances.

2. Temperatures of 8 to 10 C. for four hours have no appreciable influence on increasing the nonspecific fixation or inactivation of complement by various antigens.

3. Temperatures of 8 to 10 C. for eighteen hours greatly increase the anticomplementary activities of cholesterolized extracts and to a lesser extent of extracts of acetone-insoluble lipoids; there is less effect on the anticomplementary activity of plain alcoholic extracts.

4. Temperatures of 8 to 10 C. for from four to eighteen hours have little or no influence on increasing the anticomplementary activities of heated human serums.

5. Heating in a water-bath at 38 C. following incubation at from 8 to 10 C. for from four to eighteen hours increases the anticomplementary activities of antigens and serums.

6. Nonspecific complement-fixation reactions with mixtures of normal nonsyphilitic serums and organ extracts were not observed except in combined cold and warm primary incubations at four to eighteen hours at 8 C. plus one hour in a water-bath at 38 C.; alcoholic extracts saturated with cholesterol (0.4 per cent.) were found particularly likely to yield these reactions, whereas plain alcoholic extracts, extracts containing 0.2 per cent. cholesterol and extracts of acetone-insoluble lipoids were usually free from these nonspecific effects.

TOMLINSON, Omaha.

ELEPHANTIASIS OF GENITALS DUE TO LUES. DR. R. SCHWANK,
Ceska dermat. 1:33, 1920.

The patient, a man, aged 46, with a healthy wife and three children, negative personal and venereal history, presented a marked diffuse swelling of the penis and scrotum. The edema was painless and developed to the side of a child's head in the course of two weeks. Slight phimosis was present. There was no urethral discharge. In the dorsal surface a definite cord-like infiltration was palpable, corresponding in location to the dorsal lymph vessel. The scrotum was uniformly enlarged; the testicles and epididymis were normal. The inguinal glands were the size of a walnut, hard, smooth, freely movable, not tender. The Wassermann reaction was positive. An excised gland showed miliary gummas with a dense connective tissue infiltration almost entirely replacing the adenoid structure. Microscopic examination excluded the presence of tuberculosis by the typical vascular changes and the absence of giant cells. The author believes that advanced changes in the inguinal lymph glands, destroying almost completely the adenoid structure, were partly responsible for changes in lymph circulation, its stagnation, and the resulting edema with final elephantiasis. The process led to conditions analogous to complete extirpation of the glands. The patient improved rapidly under vigorous combined anti-syphilitic treatment. The swelling was reduced to half the original size in one month. Later it increased again somewhat, without apparent cause. The patient disappeared from further observation.

CEPELKA, Chicago.

PRECIPITATION REACTION OF SACHS AND GEORGI IN INVESTIGATION OF BLOOD AND CEREBROSPINAL FLUID. E. SALEN,
Acta dermat.-ven. 3-4:428 (Dec.) 1920.

The author made 563 blood tests, using the Wassermann and the Sachs-Georgi methods in each case, and he has classified the results in groups accord-

ing to the strength of the reaction and agreement or disagreement of the results. The results, in the main, were parallel, but in treated patients the Sachs-Georgi reaction appeared to remain positive longer than the Wassermann. In a few cases of syphilis with positive Wassermann reactions the Sachs-Georgi reaction was negative or only feebly positive. However, in the latent cases with negative Wassermann reactions, the Sachs-Georgi test was often positive in both the blood and spinal fluid. A number of nonsyphilitic patients with various diseases were also tested, and in none of them was a positive result obtained. The reaction of Sachs-Georgi, therefore, seems to be fully as specific as the Wassermann test, if not more so, and its great simplicity enables it to be performed when the older method could not be attempted. The two methods are best used in parallel, however.

Fifty-two spinal fluid tests were made likewise by both methods, and the results were parallel in 84.63 per cent. of the cases. This agrees with the results obtained by other investigators, and the percentage might have been even higher, thinks the author, had various amounts of the fluid been used in each case. For one fluid, relatively small amounts may give a typical positive reaction, and not larger amounts; for another fluid the opposite may be true. The use of larger amounts of the fluid may lead to unspecific reactions. This technic must be further refined.

PARKHURST, New York.

THE CEREBROSPINAL FLUID IN TREATED SYPHILIS. J. E. MOORE,
J. A. M. A. 76:769 (March 19) 1921.

The author examined the cerebrospinal fluid of 642 patients in all stages of syphilis, none of whom presented clinical evidence which would have justified a diagnosis of syphilis of the nervous system. These patients had received routine treatment for from two to six months.

Of thirty-four patients in whom treatment was begun before the appearance of secondary symptoms, only one showed cerebrospinal fluid abnormalities. In those patients in whom treatment was instituted after generalization had occurred, the incidence of neuraxial involvement was found to be from 12 to 15 per cent. There was no manifest difference in the percentage of involvement if treatment was begun in the secondary or tertiary stage of syphilis.

A persistently positive Wassermann reaction in the blood, slight pupillary abnormalities and certain minor complaints, such as headache, nervousness, lassitude and generalized neuralgic pains are valuable indexes of cerebrospinal complication. Twenty-eight per cent. of syphilitic patients with these signs or symptoms showed spinal fluid abnormalities, whereas only 7 per cent. of patients in whom they were absent gave evidence of neuraxial pathology.

Asymptomatic neurosyphilis is approximately twice as frequent in white as in colored patients. Speaking generally, it may be said that intensive, routine antisymphilitic treatment is capable of eradicating evidence of neurosyphilis.

Moore urges routine spinal fluid examination of all patients with syphilis.

MICHAEL, Houston, Texas.

ROENTGEN-RAY THERAPY OF SKIN CARCINOMA. K. GAWALOWSKI,
Ceska dermat. 1:233, 1920.

The theoretical part of the paper discusses the effect of roentgen rays on the neoplasm cells. According to Schwartz, their sensitiveness to rays seems to depend on their large content of lecithin (5.5 to 8 per cent. against 2.3 per

cent. in muscle fiber). The rays decompose lecithin, and its decomposition products, especially cholin, destroy the cells. Some authors believe in primary irritation of the connective tissue cells, with resulting hyperplasia of connective tissue and strangulation of cancer nests. The irritation theory would explain the rapid filling in of the defects from disintegrated tumors and the rapid healing. In discussing the quality of roentgen rays used in skin cancer, the author prefers the hard filtered rays. The question of cancer dose differs with different authors. The author describes the roentgenoscopes used in the work in Prague. The clinical part of the paper deals with the effect of the rays on different forms of skin cancer. There is usually an increase in the size of the tumor after a certain latency—ten to twelve days. With unfiltered rays or with 1 mm. aluminum the reaction is mainly superficial. In cases of crater-form epithelioma, the floor seems to come up, and the borders flatten out. Healing takes place in from three to four weeks. Pigmentation follows, and later disappearance, with desquamation. In *ulcus rodens* secretion diminishes, crusts dry up and adhere for a long time. After separation a smooth scar remains. In cases of extensive tumors, after the initial exposure a rapid disintegration takes place, as a rule. In two cases a pseudoreaction—light erythema—appeared the same day and lasted from two to four days. After hard rays, the reaction is similar but pigmentation more marked. Pseudoreactions are more common. The real reaction comes on in from ten to twelve days. The author believes that no harm can ever result from roentgenotherapy in cases of cancer if care is taken not to give "the irritant dose."

CEPELKA, Chicago.

LES TRICHOPHYTIDES (THE TRICHOPHYTIDES). B. BLOCH, *Ann. de dermat. et syph.* 1:1 and 2:55, 1921.

It has been shown that the deeper trichophyton infections are not purely local but are often disseminated throughout the system, affecting the skin as a whole and at times the internal organs also. This is manifested clinically by the appearance of the so-called trichophytides accompanied usually by fever, a leukocytosis, swelling of the lymph nodes and, occasionally, of the spleen. The biologic character of these alterations is well shown by the reaction of the organism attacked by the trichophyton to subcutaneous or intradermic injections of trichophytin, an extract of the fungus. This closely parallels the tuberculin reaction.

The author describes several trichophytides: (1) Lichen trichophytique, which often resembles lichen scrofulosorum and sometimes lichen spinulosus. The lesions consist of pale reddish follicular papules, grouped or disseminated. (2) The trichophytic erythema nodosum. (3) The trichophytic erythema scarlatiniforme. (4) Rare forms: (a) trichophytic erythema multiforme, and (b) a pustular trichophytid (impetigo trichophytique). Cases are reported in detail, with the results of trichophytin injections, 0.1 c.c. of the concentrated preparation having been administered as a dose. A considerable reaction followed the injection, with a resultant cure.

The pathogenesis of the trichophytides is discussed at some length, and it is concluded that two conditions are necessary for their occurrence: a sensitized skin and a dissolved trichophytic antigen arriving via the blood stream. In conclusion one fact is emphasized: that in the trichophyton infections, as

in other infections, the toxic and infectious material carried by the blood stream from the initial focus to the sensitized skin can provoke different dermatoses of the type of the trichophytides.

PARKHURST, New York.

NOTE ON DR. SWANK'S CASE OF EPIDERMOLYSIS BULLOSA.

F. SAMBERGER, *Ceska dermat.* 2:97, 1920.

Dr. Schwank's case shows how little is yet known about the diseases caused by the changes in the secretion or circulation of lymph. Few authors realize that the lymph is secreted by the endothelium of blood capillaries, and that it has an independent circulation in the skin. A damage to a lymph vessel will lead to outpour of lymph as damage to a blood vessel results in bleeding. A hypersecretion of lymph will cause accumulation of lymph in the affected area. Both conditions, the hypersecretion and the outpour, may cause a vesicle. When the vesicle resulting from the outpouring of lymph from an injured vessel ruptures, healing will soon take place. When the vesicle caused by the hypersecretion of lymph ruptures, it leaves a weeping erosion. Weeping lasts as long as the hypersecretion. In the production of vesicles the degree of coherence of epidermoidal cells plays an important part. The coherence of cells may be disturbed. A person can be born with decreased coherence of cells. The cells with normal coherence may be torn apart by various local or general conditions—as, for instance, in the case of dyshidrotic vesicles—the coherence is reduced by the saturation of epidermis by sweat, or by lymph in case of pemphigus. In both cases a mechanical irritation furnishes the exciting cause of vesicle formation.

Prof. Samberger does not consider Dr. Swank's case as one of epidermolysis bullosa. He reserves that term for cases characterized by formation of vesicles resulting from outpour of lymph into an epidermis with congenitally decreased intercellular coherence. In Dr. Swank's case the vesicles resulted from the hypersecretion of lymph, and the case is, therefore, one of pemphigus facticius.

CEPELKA, Chicago.

REGARDING AN UNUSUAL FORM OF MIGRATORY ERYTHEMA CAUSED BY TICK BITES. J. STRANDBERG, *Acta dermat.-ven.* 3-4:422 (Dec.) 1920.

This peculiar affection which, it is thought, may be akin to the erysipeloid of Rosenbach, has been reported several times lately before the Dermatological Society of Stockholm. The bite of a tick (*Ixodes reduncus* or *ricinus*) seemed causative in all those cases. Ehrmann (*Atlas der Hautkrankheiten*) mentions two cases of erysipeloid due to tick bites.

The patient was a girl, 4 years old, who had previously been exposed to tick bites. There then appeared a painless red swelling at the left nipple; this spread centrifugally, becoming ring-shaped. When the author saw her, two months later, the nipple was enlarged and infiltrated, being about seven-eighths inch in diameter and of a bluish red color. Around this point, at a radius of about 4 inches, ran a roughly circular band about one-eighth inch in width, which was not raised and whose red color disappeared on pressure. Between the nipple and this ring the skin was faintly erythematous and showed a fine network of faint bluish-red lines. In the left axilla were a few bean-sized painless lymph nodes. No biopsy could be secured.

The author considers the condition probably of toxic origin, spreading through the lymphatic pathways of the skin.

PARKHURST, New York.

**LATENT INFECTIONS WITH THE DEMONSTRATION OF SPIRO-
CHAETA PALLIDA IN THE LYMPHOID TISSUES OF THE
RABBIT.** WADE H. BROWN and LOUISE PEARCE, *Am. J. Syphilis* 5:1
(Jan.) 1921.

Rabbits, like human beings, following infection with syphilis arrive at a period of latency and have no demonstrable evidence of the disease. The authors therefore set about to demonstrate the infection during the period of latency and to determine the location of the spirochete during this period.

Six rabbits which had recovered from generalized syphilis were used. One had been inoculated over four years prior to examination, one nine months and the others seven months before being examined. All had been in a stage of latency of not less than three months. Popliteal lymph nodes were removed, an emulsion made from each animal, and 5 c.c. of this material were injected into the right testicle of two rabbits. All injected animals developed active lesions following an incubation period varying from thirty-one to forty-four days. It is therefore concluded that rabbits which have recovered from the clinical evidence of syphilis may harbor virulent organisms.

The apparent infectivity of lymph node material, together with other evidence of the selective action of spirochetes for this tissue, would seem to indicate that the lymphoid tissues are the chief reservoirs of the virus.

TOMLINSON, Omaha.

ACTINOMYCOSIS ATYPICA. K. HUBSCHMANN, *Ceska dermat.* 1:185, 1920.

A schoolgirl, aged 14, had a negative family and personal history. Her trouble started during the wheat threshing time. Her skin lesion was undoubtedly secondary to the infection of a carious tooth. The possibility of a primary salivary gland infection was excluded. The skin lesion occupied a large part of the right cheek between the outer canthus and the lobe of the ear. Under potassium iodid internally, roentgen-ray therapy, and local applications of a 10 per cent. solution of potassium iodid in the form of compresses, the patient improved remarkably.

After extensive cultural work and examination of many specimens, the author considers the case one caused by an atypical actinomyces, some transitional form between actinomyces and streptothrix, according to Petruschky's classification. The patient was given an intradermic injection of antigen prepared from a two-months-old gluco-maltose bouillon culture. A marked local reaction took place. There was no rise in temperature. The second day after the injection, the actinomycotic area became red, swollen and very tender. There was an increase in the discharge of pus, rich in granules. The focal reaction subsided in fourteen days.

CEPELKA, Chicago.

**LICHEN PLANUS OF TONGUE IN SYPHILITIC PATIENT UNDER
ARSENICAL TREATMENT; ERYTHEMATOUS OUTBREAKS
AFTER ARSENICAL INJECTIONS LEAVING PIGMENTED
PLAQUES.** L. QUEYRAT and RABUT, *Bull. Soc. franç. de dermat. et
syph.* 2:39, 1921.

A woman, aged 25 years, had first received neo-arsphenamin in local applications for Vincent's angina; later an intravenous dose was given. A subsequent Wassermann reaction was positive, and a course of galyl injections was begun; after the twelfth injection a pruriginous eruption of red plaques

appeared and persisted for fifteen days without fever or constitutional disturbance. Later, intravenous injections of the sanar brand of neo-arsphenamin were administered for the relief of oral lesions which were thought to be leukoplakia; they were subsequently found to be lichen planus, clinically and histologically. While receiving different kinds of arsenical medication, she had several attacks of this erythematous eruption, from which pigmented plaques remained.

She also presented a keratoderma palmaris et plantaris, probably congenital. Darier confirms this diagnosis.

Thibierge has lately presented a case of erythematous and pigmented eruption following neo-arsphenamin therapy, and a similar case is at present under his observation.

PARKHURST, New York.

THE EFFECT OF CARBONIC ACID GAS ON THE SKIN. F. SAMBERGER, *Ceska dermat.* 2:1, 1920.

Bathing in water containing free carbonic acid gas causes redness and a sensation of warmth in the skin. The author's theory explaining this action is based on the physiologic fact of cutaneous respiration which he demonstrated in his previous works. Under normal conditions the corium takes its oxygen supply from the external air (not from the lungs) by means of capillaries in the papillary region, both ascending and descending loop being arterial. This physiologic function can be disturbed by lowering the amount of surrounding oxygen. The skin finds itself in a condition of air hunger, and the circulation in respiratory capillaries accelerates. This acceleration becomes greater the more completely the external supply of oxygen is eliminated. The increased circulation is accompanied by production of heat sensation in the skin without any other changes in the appearance of the skin. (The color of the skin depends on the deep vascular changes.) If the external oxygen is completely shut off, the skin has to take it up from the next available source, namely, the deep vascular plexus situated between the corium and subcutis, carrying oxygen from the lungs. The skin of a patient immersed in a bath charged with free carbonic acid gas soon becomes covered with bubbles of gas, and finds itself, therefore, in an irrespirable atmosphere. To supply the needed oxygen the deep arterial plexus joins in active dilation—and the skin reddens. This knowledge of the effect of carbonic acid gas on the skin and capillaries explains its effect on general circulation.

CEPELKA, Chicago.

OBSERVATION OF THIRTY-FIVE CASES OF TROPICAL PHAGEDENIC ULCER. CLEMENT, *Bull. Soc. franç. de dermat. et syph.* 2:64, 1921.

These cases were observed in the tropics, especially in Senegal. The ulcers were sloughing, with raised indurated borders. They involved not only the soft parts but also the tendons, joints and bones. The onset of the lesion appeared as a pustule, and the odor of the fully developed ulcer is described as cadaveric. Insect bites, scratches and similar traumas furnished the evident portal of entry. In almost every case a spirillum and a fusiform bacillus were found, not identical with the organisms of Vincent. The Wassermann reaction may be temporarily positive. Purely local treatment, by curettage with the application of

iodoform fumes, brought about a complete cure within from fifteen to fifty days. The cases with joint involvement were more protracted, but all patients were cured.

PARKHURST, New York.

PIAN DES MUQUEUSES (YAWS OF THE MUCOSAE). P. NOEL, *Ann. de dermat. et syph.* 2:72, 1921.

In a review of the literature concerning yaws, the author found that little or no consideration is given the so-called primary and secondary lesions of the mucosae. He, therefore, reports the results of a complete examination in 100 successive cases of the disease which came under his care. In thirty-seven of these cases the mucosae were involved, the oral mucosa in twenty-two, the nasal in nineteen and the conjunctival in four.

The usual mucous lesions are sharply margined oval patches, pale red and slightly roughened or papillomatous. They are soft and noninfiltrated, and bleed readily on pressure; when occurring in the commissures they are often fissured. Pain is not a prominent symptom. They often correspond to points of dental pressure. Only one lingual lesion was observed; it appeared in a patient with many other lesions of the mucosae, and was described as being a small tumor 6 mm. in diameter with elevated pale border and a depressed red center. In the nose the lesions are large and papillomatous, with yellowish crusts; they bleed readily, and if numerous, obstruct the nasal respiration. Conjunctival manifestations are considered rare; they resemble those of the buccal mucosae. They usually heal spontaneously and leave no trace.

Verruca peruana, gangosa and syphilis must be ruled out. However, cutaneous lesions are nearly always present, usually on the legs, but often on the arms, genitals, trunk or face. The vast majority of the patients are under 30 years of age (97 of the author's 100).

By way of treatment galyl and neo-arsphenamin are preferred.

PARKHURST, New York.

ON CREEPING DISEASE. HARUKICHI TAMURA, *Brit. J. Dermat. & Syph.* 33:81 (March) 1921.

Tamura describes an interesting case of creeping disease in which the parasite was recovered and found to belong to the genus *Gnathostoma*, and probably of the *siamense* species. This parasite is a zoologic curiosity in itself, being found rarely in Japan; it has never before been known to invade the human skin. All cases of creeping disease reported heretofore have been thought to be due to the *Gastrophilus* larva, although the parasite has been recovered in only six of the forty-three cases reported.

The author was able to watch the travel of the parasite almost from the start, and he describes its course carefully. The lesion was excised after the *Gnathostoma* had been extracted, and serial sections made. It was found that the tunnel was in part within the epithelium, and in part between the epithelium and corium. In nearly all other cases of creeping disease the epidermis only has been invaded, although the corium has been reported invaded in one instance. There is a careful description of the parasite, and of the histopathologic changes produced in the skin by it. Thirty-eight of the reported cases of creeping eruption are summarized. The article is to be continued.

SENEAR, Chicago.

ATROPHIA CUTIS IDIOPATHICA CHRONICA PROGRESSIVA DIFFUSA. B. REJSEK, Ceska dermat. 1:209, 1920.

The patient, a woman, aged 34, showed an idiopathic atrophy of the skin which had begun at the age of 18, developing symmetrically on the dorsal parts of both feet and spreading toward the lower third of the thighs. She used various local applications and arsenic internally without effect. At the time of examination she showed a well advanced case of atrophy of the skin with disappearance of the hair and follicular orifices. Underlying vascular plexuses were plainly visible.

The author describes in detail the histologic findings of sections of the skin, showing the earliest and the most advanced changes. He considers the vascular changes (thickening of the intima, infiltration of the adventitia of the larger vessels) as primary and most important. The cellular infiltration follows with changes in the connective tissue, and final disappearance of the elastic fibers. In advanced cases the stratum papillaris is completely gone. The article contains a review of various theories dealing with etiology. The patient showed considerable improvement after 30 gm. of potassium iodid had been taken. The infiltration present on both shins disappeared, the skin became pliable and less livid, and scaling lessened. The atrophic areas felt definitely firmer to touch.

CEPELKA, Chicago.

FIEVRE SYPHILITIQUE PRIMAIRE (FEVER IN THE PRIMARY STAGE OF SYPHILIS). MILIAN and MOUQUIN, Bull. soc. franç. de dermat. et syph. 9:361, 1920.

Among twenty-one patients an irregular temperature curve approximating 38 C. was observed in four, whose chancres were of seven, fourteen, sixteen and twenty-one days' duration, respectively. A complete physical examination revealed nothing, except in the patient whose chancre was of seven days' duration. This patient complained of headache so severe as to prevent sleep; there was parietal tenderness, and the spinal fluid, though otherwise normal, contained, on the thirteenth day, 13 lymphocytes per cubic millimeter. Mercury cyanid was injected in one case, and a Herxheimer reaction followed.

PARKHURST, New York.

KLINISCHE ERFAHRUNGEN MIT DEM BENKOESEN IODPRAEPARAT (CLINICAL EXPERIENCE WITH BENKOE'S IODIN PREPARATION). J. KYRLE and H. PLANNER, Wien. klin. Wchnschr. 34:106, 1921.

The gist of the report of 6,000 injections, in nearly 400 patients, is that "Mirion" is nontoxic. As it was used only in combination with arsphenamin, it is not feasible at this time to give any definite statement as to its ultimate value in the treatment of the disease. Special chapters are devoted to the fact that injections of the preparation excite so-called Herxheimer reactions, and that it has also provoked positive Wassermann reactions in treated cases. "Mirion" is given intramuscularly in 5 cm. doses, and it may also be given intravenously. A course includes from twenty to forty injections.

GOODMAN, New York.

A NOTE ON THE TREATMENT OF ERYSIPELAS WITH BRILLIANT GREEN. J. E. ADAMS, Brit. M. J. 2:779 (Nov. 20) 1920.

The author reports some unusually good results in the treatment of cutaneous erysipelas with a solution of brilliant green. In a dozen cases so treated the average time for subsidence of the attack was just over five days. The method employed was to paint the affected area with a 5 per cent. aqueous solution once a day in mild cases and twice a day in severe ones. The only objection to the use of this remedy has been the staining. When the eruption has subsided, the discoloration can be removed in three or four days by vigorous washing, preferably with ether soap.

OLIVER, Chicago.

ATROPHODERMIE VERMICULEE DES JOUES AVEC KERATOSES FOLLICULAIRES (VERMICULATED ATROPHODERMIA OF THE CHEEKS WITH FOLLICULAR KERATOSES). J. DARIER, Bull. soc. franç. de dermat. et syph. 9:345, 1920.

A child, aged 9 years, presented this interesting condition, so well described by MacKee and Paroungian in the *Journal of Cutaneous Diseases*, 1918, page 339, under the name "Folliculitis ulerythematosia reticulata." Histologic examination revealed: (1) a sclerosing atrophy, especially perifollicular, with important changes in the elastic tissue comparable to those found in partial scleroderma; (2) follicular changes consisting of deformity with cystic "buds" and a keratosis at the mouth of the follicle that bore some resemblance to a comedone. Darier considers the term "vermiculated atrophoderma" to be the best descriptive name, both clinically and histologically. Two excellent pictures of the case, and also a histologic section, are reproduced.

The condition was benefited greatly by a three months' vacation at the seashore, the improvement being attributed to the ultraviolet rays of the sunlight.

PARKHURST, New York.

A CASE OF LOCALIZED ARGYRIA. B. B. BEESON, J. A. M. A. 76:1006 (April 9) 1921.

The patient had treated some pimples on his nose by boring into them with a silver nitrate crayon once a month for about a year. Several months later discoloration of the nose became noticeable. This increased in intensity until the part became bluish black in color. No changes, other than that of pigmentation, were present.

MICHAEL, Houston, Texas.

SYPHILIS AS AN ETIOLOGIC FACTOR IN NODULAR CIRRHOSIS OF THE LIVER. L. J. OWEN, Am. J. Syphilis 5:20 (Jan.) 1921.

Data for this report were obtained from a review of 1,200 necropsy examinations performed at the Washington University School of Medicine. It was found that 8.5 per cent. of all adults had cirrhosis of the liver, and of these 80 per cent. had the nodular type of cirrhosis. Basing a diagnosis of syphilis on either clinical evidence, serologic findings, history or a combination of these, this disease was found associated with 40 per cent. of cases showing nodular cirrhosis. Alcoholism and syphilis were commonly associated.

Chronic infectious processes, such as chronic arthritis and endocarditis, were found to be sufficiently frequent to warrant further investigation of their etiologic importance.

TOMLINSON, Omaha.

PSEUDO-ICTERIC XANTHOSIS. F. PARKES WEBER, Brit. J. Dermat. & Syph. **33**:103 (March) 1921.

Weber reviews those conditions which give rise to "pseudo-icteric" pictures. Racial factors, coloration resulting from consumption of picric acid, carotinemia and pseudo-icteric diffuse yellowness, or "xanthosis" of the skin, occurring in patients suffering from diabetes mellitus, are discussed briefly.

The author then reports a case of congenital xanthosis involving the sclerotics in an otherwise healthy man. The patient, 54 years of age, active, well built and well nourished, had been (according to his mother), yellow at birth, and had remained more or less yellow. The sclerotics were affected, as well as the skin. Physical and laboratory examinations revealed only negative results. There were no other cases in the patient's antecedents, and four children were unaffected. The patient has been under observation for four years.

SENEAR, Chicago.

SYNDROME DE MIKULICZ FRUSTE A LOCALISATION BI-PAROTIDIENNE CHEZ UN SYPHILITIQUE SECONDAIRE (INCOMPLETE SYNDROME OF MIKULICZ LOCALIZED IN BOTH PAROTID GLANDS, IN A PATIENT WITH SECONDARY SYPHILIS). C. FLANDIN and AUBIN (J. DARIER), Bull. soc. franç. de dermat. et syph. **9**:352, 1920.

A man, aged 24, presented a painless swelling of both parotids which had insidiously developed since the third month of his untreated syphilitic infection. There was no modification of the salivary function, nor were any other salivary or lacrimal glands involved. It was therefore considered to represent an abortive type of the Mikulicz syndrome, probably syphilitic in origin. Treatment would decide this.

PARKHURST, New York.

HYPOCHLORHYDRIA, A POSSIBLE CAUSE OF PERSISTENT ERYTHEMA MULTIFORME. A. SCHALEK, J. A. M. A. **76**: 1005 (April 9) 1921.

Schalek's two patients had a severe, persistent type of the disease, which had resisted various methods of treatment. It was determined by gastric analysis that each patient had hypochlorhydria, and on the administration of twenty drops of dilute hydrochloric acid after meals, the eruption promptly disappeared.

The author suggests that the striking results obtained warrant further investigation along the same line.

MICHAEL, Houston, Texas.

PIGMENTATION RETICULEE DES CUISSES DUE A LA CHALEUR (RETICULATED PIGMENTATION OF THE THIGHS DUE TO HEAT). C. DU BOIS, Ann. de dermat. et syph. **2**:82, 1921.

Montpellier of Algiers has recently described a pigmentation of the thighs of native women whose custom it is, during the winter, to carry a small stove between their legs. In rural France a similar stove is used, the author states, and with the same result. The pigmentation is reticulated, and at first disappears during the summer when the heater is not in use, but with advancing years it tends to persist throughout all seasons.

(Montpellier's article appeared in the *Annales*, July, 1919.)

PARKHURST, New York.

PSORIASIS TRAITES PAR UNE PREPARATION NOUVELLE: LE PROCUTA (A NEW PREPARATION FOR THE TREATMENT OF PSORIASIS: PROCUTA). L. Brocq, Bull. soc. franç. de dermat. et syph. **9**:342, 1920.

A Parisian pharmacist has devised a mild and relatively nonirritating product, procutine, which is a sulphur-chrysophanic acid combination containing 20 per cent. of sulphur. It may be prescribed in a number of combinations, the ointment called procuta having the following ingredients:

Chrysophanic acid and sulphur (procutine).....	10
White petrolatum	850
Paraffin	150

It is useful as an ointment for general application, but a stronger preparation is necessary to remove the inveterate lesions. Brocq has tried it to his satisfaction, although in one case a mild conjunctivitis resulted.

PARKHURST, New York.

JUVENILE TABES. H. L. PARKER, Arch. Neurol & Psychiat. **5**:122 (Feb.) 1921.

In an interesting article the author carefully reviews the literature on juvenile tabes and reports ten cases of the disease from the Mayo Clinic.

Juvenile tabes is now a well recognized entity, and with our increased facility of diagnosis, more and more cases are being recognized and reported. The features of the disease are the insidious onset, the lengthy and even latent course of the disease, the frequency of optic atrophy with blindness, and the frequency of incontinence of urine. The relative rarity of ataxia, girdle sensations, and lightning pain, and the frequent paretic termination are features that stamp juvenile tabes with a distinctive mark and distinguish it from the adult type.

OLIVER, Chicago.

SUR UNE DERMATOSE (TUBERCULIDE?) CONSTITUEE PAR DES ELEMENTS ERUPTIFS SUCCESSIFS PIGMENTES, ERYTHEMATO- ET PAPULO- PIGMENTES. ET MOLLUSCIFORMES (REGARDING A DERMATOSIS [TUBERCULIDE?] MADE UP OF ERUPTIVE ELEMENTS SUCCESSIVELY PIGMENTED, ERYTHEMATO- AND PAPULO-PIGMENTED AND MOLLUSCIFORM). C. AUDRY and BERTUCAT, Ann. de dermat. et syph. **2**:49, 1921.

A girl, aged 18 years, whose mother had died of pulmonary tuberculosis, gave an otherwise negative history and presented no internal abnormalities except a slightly enlarged spleen. For four years her trunk and arms had been the site of an eruption whose only subjective accompaniment was a mild nocturnal pruritus. The scattered lesions often attained a diameter of 3 cm., and they were primarily brownish macules of anetodermic appearance. Later they became erythematous and papular, and finally mollusciform. They disappeared after the application of caustics, leaving keloidal scars. Histologically, at first the lesions were essentially atrophic, degenerative and pigmented. Then a small perivascular lymphocytic infiltration appeared, without nodular arrangements or plasma cells, and finally a soft fibroblastic organization occurred.

The authors consider the eruption to be probably a tuberculid. It was impossible for them to examine the patient's blood or to make a tuberculin test.

PARKHURST, New York.

FEEBLEMINDEDNESS IN HEREDITARY SYPHILIS. O. J. RAEDER, Am. J. Dis. Child. **21**:240 (March) 1921.

This article reports the results obtained in a study of thirty cases of hereditary neurosyphilis. The series of cases consisted of thirty children ranging in age from 2 to 16 years, in either one or both of whose parents there was a positive Wassermann reaction on the blood serum. Most of the parents had neurosyphilis of the paretic type.

Blood and spinal fluid examinations were made on twenty-two of these children. It was found that various degrees of syphilitic infection are present in a definite order in a family of several children, the oldest, born soonest after the parental infection, showing the greatest injury and the succeeding children showing milder degrees in order. Psychometric examinations revealed corresponding psychic terracing going *pari passu* with the grades of physical defect.

The youngest children of a family, though seronegative, have been found to be feeble-minded to a slight degree. The syphilitic injury to the nervous system projects beyond the physical defect, or by reason of the peculiar reactions of the brain compared with other organs, we have a finer indicator in it than in ordinary tissues. Mental deficiency in congenitally syphilitic children not of feeble-minded parents is in the majority of cases due to syphilis.

OLIVER, Chicago.

TUBERCULIDES MULTIPLES DES MEMBRES INFERIEURS A TENDANCE ATROPHIQUE (MULTIPLE TUBERCULIDS OF THE LOWER EXTREMITIES WITH A TENDENCY TO ATROPHY). G. THIBIERGE and P. LEGRAIN, Bull. soc. franç. de dermat. et syph. **9**:354, 1920.

This case had been previously presented (in the Bulletin, p. 261, 1920) as "A Circinate Dermatositis with Atrophic Center, Multiple Elements, of Undetermined Nature." The histologic examination at that time favored a diagnosis of syphilis, but Darier considered it to be a tuberculid, and his conviction was borne out therapeutically, four tuberculin injections producing immediate relief.

PARKHURST, New York.

THE FOUR STAGES OF SYPHILIS. A. BRAUER, Arch. f. Dermat. u. Syph. **126**:311, 1918.

Brauer, on field service with the army, writes a more or less philosophical paper on the relation of *Spirochaeta pallida* and the tissue reactions of the host. The more recent experimental work of Arzt and Kerl, and of Brown and Pearce makes most of the former conceptions of syphilis antiquated.

GOODMAN, New York.

MILK INJECTIONS IN TREATMENT OF GONORRHEAL COMPLI-CATIONS. SIEGFRIED GELLIS, and JOSEF WINTER, Arch. f. Dermat. u. Syph. **126**:267, 1918.

This article is mentioned here only because it may prove a reference to those interested who have not been able to follow the recent foreign, especially German, literature. Nonspecific therapy, as for example milk, has also been proposed for syphilis.

GOODMAN, New York.

CAMEL ITCH. W. DYSON, Brit. J. Dermat. & Syph. **33**:107 (March) 1921.

Dyson reports an epidemic of skin diseases among the camel corps in Palestine in 1917. The eruption was a papular, intensely irritative dermatitis, follicular and similar to that caused by the harvest bug (*Leptus autumnalis*). Investigation of scrapings from the skin of the patients and scrapings from the skin of animals suffering with mange showed that the dermatitis was caused by a parasite similar to, but smaller than, *Acarus scabiei*, which entered the skin by burrowing down a hair follicle.

Since this parasite does not propagate its kind on the human skin, it was only necessary to avoid contact with mangy camels and to prescribe an anti-pruritic remedy.

SENEAR, Chicago.

EPIBULBAR CARCINOMA; ANGIOSARCOMA OF LID. GEORGE E. DESCHWEINITZ, Am. J. Ophth. **4**:91 (Feb.) 1921.

A traumatic conjunctivitis of long standing produced by direct injury was followed in three years by the development of a papilloma of the corneoscleral margin. Microscopic section of the papilloma showed one area resembling pearly body formation. The squamous cell carcinoma observed nine years later originated on the site of the previous lesion. The not infrequent occurrence of such sequelae is alluded to, as is also the prophylactic value of radium.

2. The lesion, resembling a cavernous angioma of the eyelid and proving to be a spindle cell hemangioma, is the earliest recorded case of this type, the patient being 5 months old. A 15 mm. radium tube was applied on the line of incision for ten hours.

FOERSTER, Milwaukee.

LE ROLE DETERMINANT DE LA PONCTION LOMBAIRE DANS CERTAINES MENINGITES SYPHILITIQUES DE LA PERIODE SECONDAIRE (THE DETERMINING ROLE OF LUMBAR PUNCTURE IN CERTAIN CASES OF SYPHILITIC MENINGITIS IN THE SECONDARY PERIOD). M. GOUBEAU, Bull. soc. franç. de dermat. et syph. **9**:357, 1920.

There were presented six cases of secondary syphilitic meningitis following lumbar puncture in patients who had presented no preceding clinical or laboratory signs of meningeal involvement, their spinal fluids having been negative at the time of the puncture. Goubeau therefore urges that lumbar puncture at this period be practiced only with prudence and when absolutely indispensable. The prognosis in these cases, however, is excellent for immediate recovery, if energetic treatment is used.

PARKHURST, New York.

SPECIFIC INHIBITORY REACTION OF CHOLESTERINIZED ANTIGENS IN THE WASSERMANN TEST. WILLIAM A. HINTON, Am. J. Syphilis **5**:81 (Jan.) 1921.

From a study covering several years, during which time 150,000 reactions were performed, the author concludes that "when used with a suitably standardized hemolytic system, carefully selected cholesterolized antigens have high specific inhibitory reaction and are superior to the plain extracts artificially prepared lipoids."

TOMLINSON, Omaha.

PIGMENTAZIONE DI LESIONI CUTANEE DA DERMATOFITI CROMOGENI (CUTANEOUS PIGMENTATION DUE TO DERMATOPHYTON). C. LOMBARDI, *Riforma med.* **37**:154 (Feb.) 1921.

Many dermatophytoses are pigment producers, but pigmentation rarely occurs in vivo, except in cases of caratè or pinta and a few tropical dermatophytoses. The patient in the case reported by the author presented several yellowish-brown squamous lesions scattered over the hands and arms. On microscopic examination the scales showed abundant mycelium and numerous granules of pigment. Cultures on Sabouraud's medium identified the fungus as the *Tricophyton faviforme ochraceum*.

PARDO-CASTELLO, Havana.

SUPERNUMERARY BREAST ON BUTTOCK. P. A. PERKINS, J. A. M. A. **76**:792 (March 19) 1921.

The patient, a man aged 59 years, presented an orange-sized tumor surmounted by a well developed nipple, on the right buttock. The patient stated that his attention was first attracted to the tumor when he was 17 years old, at which time a whitish secretion exuded from the nipple. The secretion later became prune juice colored and occurred monthly, lasting for a few days. When he was 37 years old the secretion ceased.

There were no other developmental abnormalities.

MICHAEL, Houston, Texas.

SIGNIFICANCE OF SYPHILIS AS AN ETIOLOGICAL FACTOR IN ACUTE IRITIS. C. A. CLAPP, *Am. J. Ophth.* **4**:194 (March) 1921.

This article is a report of 100 cases of acute iritis, in 80 per cent. of which syphilis was found to be the etiologic factor, the diagnoses being based on the Wassermann reaction, presence of condylomas and the therapeutic tests. Eight per cent. of the patients had condylomas. Sixty-eight out of eighty-seven clinic patients were colored, while of thirteen private cases (twelve white) 69 per cent. proved to be syphilitic.

FOERSTER, Milwaukee.

ICHTHYOL IN THE TREATMENT OF ERYSIPELAS. EISLER, *Ceska dermat.* **1**:146, 1920.

For the last six months pure ichthyol has been used exclusively in the treatment of erysipelas on Prof. Samberger's service. There were ninety-six cases. Pure ichthyol is spread over the affected area, and about 2 to 5 cm. beyond it. The entire surface is dotted with small bits of cotton. In hardening, ichthyol incorporates the cotton and makes a protective dressing, adhering well to the skin. No bandaging is necessary. One application is sufficient. In most cases there is no tendency to peripheral extension. The temperature drops, symptoms disappear, and erysipelas clears up in five days. Internally 0.4 gm. of quinin hydrochlorid are given daily.

Samberger believes that the good local effect of ichthyol depends on its antibacterial and capillarotonic property.

CEPELKA, Chicago.

HARLEQUIN FOETUS (HYPERKERATOSIS CONGENITALIS). J. T. McAUSLIN, *Brit. M. J.* **1**:155 (Jan. 29) 1921.

The author reports a case of this rare condition. It was a full time fetus, born dead. The skin was dead white in color, cornified and cracked in all

directions, making it appear as if clad in a horny armor. Removal of a portion of skin showed a red, raw area beneath. The eyes appeared as two sacs filled with blood. There was no differentiation into the various parts, iris, pupil, etc. Postmortem examination showed a thymus of normal size, but containing a number of small scattered abscesses.

OLIVER, Chicago.

TREATMENT OF FURUNCULOSIS. DR. SVESTK, *Ceska dermat.* **1**:133, 1920.

At the skin clinic in Prague from 5 to 10 per cent. of liquor formaldehydi in a soapy base (capocreme formalin of Prof. Samberger) has been used with good results. The preparation sticks to the skin and has both an antiparasitic and astringent effect. It is rubbed gently into the lesions and neighboring skin twice daily. Besides the local treatment, four intramuscular injections of 2 c.c. each of staphylococci vaccine are given.

CEPELKA, Chicago.

DEBUT PROBABLE D'ACRODERMATITE CONTINUE SUPPURATIVE DE HALLOPEAU CHEZ UN ENFANT DE 5 ANS (PROBABLE ONSET OF THE CONTINUOUS SUPPURATIVE ACRODERMATITIS OF HALLOPEAU IN A CHILD OF 5 YEARS). G. THIBIERGE and P. LEGRAIN, *Bull. soc. franç. de dermat. et syph.* **9**:356, 1920.

A boy, aged 5 years, presented lesions of the terminal phalanges of several fingers, especially peri-ungual, and with resulting nail deformities. There were no subjective symptoms. Quick recovery followed the application of a collargol ointment, according to a subsequent report.

PARKHURST, New York.

ULCERATING GRANULOMA OF THE PUDENDA CURED BY INTRAMUSCULAR INJECTIONS OF ANTIMONY TARTRATE. H. L. CUMMING, *Brit. M. J.* **2**:775 (Nov. 20) 1920.

The author reports the cure of a stubborn case of this disease by injections of Castellani's solution of antimony tartrate with phenol and glycerin. The dosage varied between $\frac{1}{4}$ and $\frac{1}{6}$ grain. The patient was also given a solution of tartar emetic by mouth. Twelve injections were given, and about 3 grains of antimony tartrate were injected intramuscularly over a period of thirty-six days.

OLIVER, Chicago.

LEUCO-MELANODERMIE SYPHILITIQUE DU SCROTUM, SIMULANT LE VITILIGO (SYPHILITIC LEUKOMELANODERMIA OF THE SCROTUM, SIMULATING VITILIGO). J. DARIER and M. FERRAND, *Bull. soc. franç. de dermat. et syph.* **9**:350, 1920.

This manifestation followed a papulosquamous and crusted, ulcerating secondary syphiloderm, which had vanished under vigorous combined treatment. Hudelo reports that he has lately seen a similar case.

PARKHURST, New York.

NEUE WEGE IN DER SYPHILISTHERAPIE (ADVANCES IN THE THERAPY OF SYPHILIS). ALFRED FROELICH, *Wien. klin. Wchnschr.* **34**:105, 1921.

This is a preliminary communication regarding pharmacologic investigations of a new iodine compound devised by a Dr. Benkoe. It is frankly stated

that because of delay in securing patent rights, the formula, mode of preparation, etc., cannot be given. The name of the new preparation from which much is supposed to be expected is "Mirion."

GOODMAN, New York.

FRENCH ARSENOBENZOL OR GALYL. EISLER, *Ceska dermat.* **1**:202, 1920.

Galyl was tried out at the dermatologic clinic in Prague with good results in cases of malignant syphilis and early tabes dorsalis. Given to moribund patients, it proved to be an excellent roborans, well tolerated and valuable in preparing the patient for further specific treatment. Given in large amounts, it is equivalent to neo-arsphenamin, and it is superior to the latter in its absolute safety and its ease of administration.

CEPELKA, Chicago.

DIE SCHNELLBEHANDLUNG DER KRAETZE (RAPID TREATMENT OF SCABIES). MORIZ OPPENHEIM, *Wien. klin. Wchnschr.* **34**:94, 1921.

Oppenheim adds nothing new to the paper written last year and abstracted in the ARCHIVES. The incidence of scabies is still on the increase. The Wilhelm Hospital has treated 14,676 patients from September, 1918, to September, 1919, and 21,697 in the year ending September, 1920.

GOODMAN, New York.

HYPOTRICHOSIS UNIVERSALIS CONGENITA. BAZANT and GAWALOWSKI, *Ceska dermat.* **1**:174, 1920.

A farmer, aged 26, had no hair on his body. The patient's family history showed that he inherited his anomaly from the mother's side. The patient's mother had no hair, eyelashes nor brows. Her father had a universal alopecia. Two of her brothers were bald, one normal. The families of the mother's brothers show: first, normal, six children all normal; second, bald, five children, four normal and one bald, a girl; third, bald, four children, three normal and one bald, a boy. Their grandchildren are all normal. The patient has three normal brothers, two bald brothers, and two bald sisters.

The patient complained of hyperhidrosis over his entire body except on the chest. Physical examination was negative, genitalia and sexual function were normal, and there was no enlargement of the thyroid.

CEPELKA, Chicago.

X-RAY TREATMENT OF ACNE VULGARIS. W. B. WITHERBEE and JOHN REMER, *Med. Rec.* **99**:482 (March) 1921.

No local medicinal treatment should be used during treatment with the roentgen ray. The authors recommend $\frac{1}{4}$ skin units at weekly intervals for from twelve to sixteen treatments, this number to be used even though all symptoms have disappeared following eight or ten treatments.

TOMLINSON, Omaha.

USE OF RESORCIN IN SYCOSIS TRICHOPHYTICA. DR. V. SVETSKA, *Ceska dermat.* **1**:23, 1920.

A 1 to 2 per cent. aqueous solution of resorcin has been used with success in the treatment of sycosis at the dermatologic clinic of Prague. The patient is instructed to pour off a part of the solution in a dish, heat it, and dab it on the diseased area, by means of a cotton pledget, as hot as he can stand it for

five minutes, three times daily; then dry the skin gently. No bandaging is allowed, and the patient must not shave. Epilation is recommended.

Resorcin acts as an antiparasitic, an astringent and a keratoplastic. Heat aids the healing tendency.

CEPELKA, Chicago.

PRIMARY EPIBULBAR CARCINOMA. F. P. CALHOUN, *Am. J. Ophth.* **4**:101 (Feb.) 1921.

A hazelnut sized basal cell carcinoma of the lower lid was excised and 20 mg. of radium applied for one and one-half hours. The treatment was repeated for two hours in two weeks, and again in two weeks for two and one-half hours. One year later there was a recurrence in the lid, the size of a rice grain, and a metastatic gland in front of the ear.

FOERSTER, Milwaukee.

A RARE CASE OF ALBINISM. V. SVESTKA, *Ceska dermat.* **1**:171, 1920.

A girl, aged 12, with blue eyes, showed a head covered with thin, ashy blond, very soft and curly hair. The curls presented wrinkling like that seen in the hair of colored people. The hair resisted all attempts at straightening. It was elliptical on cross section. The possibility of admixture of negro blood in the ancestry was excluded. It is a question whether the case should be considered as one of albinism-negro variety or a case of atavism.

CEPELKA, Chicago.

ALKALI TOLERANCE IN PELLAGRA. M. X. SULLIVAN, *J. A. M. A.* **76**:1002 (April 9) 1921.

Sellards' method was used to determine the alkali tolerance of fifteen patients with pellagra. Four patients showed an increase in tolerance to sodium bicarbonate. Of these four patients, only two showed a marked tolerance, and they had a severe diarrhea.

MICHAEL, Houston, Texas.

THE STUDY OF ANTIGENS IN THE BORDET-WASSERMANN REACTION. F. BERKA, *Ceska dermat.* **1**:161, 1920.

Commercial products not being available during the past year, each serologic station had to depend on its own reagents. The antigens made from specific organs did not prove superior to those made from animal organs. The author concludes that all antigens can be of good use if properly titrated so that their nature is well known, and the correct dose is found.

CEPELKA, Chicago.

PRIMARY SYPHILIS—EARLY DIAGNOSIS. C. GUY LANE, *Am. J. Syphilis* **5**:87 (Jan.) 1921.

After briefly discussing the magnitude of the syphilis problem from a public health standpoint, the author emphasizes the necessity of early diagnosis, particularly by means of dark-field examination. Dark-field technic is described, and a brief discussion of early therapeutic measures is given.

TOMLINSON, Omaha.

BLASTOMYCOSIS. V. SVESTKA, Ceska dermat. **1**:137, 1920.

Considering the fact that the existence of blastomycosis in Bohemia was not generally recognized by the profession at large, the article calls attention to the four patients treated at the dermatologic clinic in Prague within a year. The lesions were situated on the exposed parts of the body, the face and the distal parts of the extremities.

CEPELKA, Chicago.

STRAIN IN SPIROCHETES. BURTON PETER THOM, Am. J. Syphilis **5**:9 (Jan.) 1921.

The author discusses the relative merits of the claims of various writers both for and against the belief of strains in spirochetes and sets forth his own ideas in support of opposition to such belief.

TOMLINSON, Omaha.

DERMATOLOGIC ABSTRACTS

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

JAUNDICE AFTER ARSENICAL TREATMENT. L. BROCCQ, Bull. méd. **35**:235 (Feb. 26) 1921.

Broccq admits that neo-arsphenamin injected in rather large doses by the vein passes directly to the liver through the hepatic artery, and is liable to induce toxic injury, with resulting jaundice. This subsides if the drug is suspended. On the other hand, the toxic injury of the liver reduces its resisting power, and thus the spirochetes are enabled to settle in the liver and thus damage the liver further. This damage is arrested by giving more arsphenamin. Subcutaneous injection of the drug does not reach the liver so directly, and hence does not entail these paradoxical effects on the liver. The toxic injury from the arsenical may be slight and transient, but, he adds, it is only with grave apprehensions that he resumes intravenous injections of neo-arsphenamin in a case in which there have already been disturbances on the part of the liver after its administration. He says that he prefers to change to mercury or to give the arsenical subcutaneously, acknowledging, *Je sais que je suis un timoré*. If the toxic symptoms predominate, the further use of the arsenical will aggravate them. If the syphilis element predominates, it will cure. He adds, "When we think of the long time it took before we learned of all the possible misdeeds of such common drugs as the salicylates, antipyrin, orthoform, etc., we feel more respect for the toxic substances which at present we are injecting by the vein in large doses, chasing the microbe without worrying as to the possible injurious action on the tissues."

SQUAMOUS CELL EPITHELIOMA OF SKIN. A. C. BRODERS, Ann. Surg. **73**:141 (Feb.) 1921.

The 256 cases in the series of squamous cell epitheliomas of the skin studied by Broders represent 12.8 per cent. of 2,000 cases of general epithelioma observed in the Mayo Clinic from Nov. 1, 1904, to July 22, 1915. Farmers represented 53.96 per cent. of the cases in males. The site of the cancer was preceded by a mole, wart, pimple, scab, ulcer, leukoplakia, crack, wen, blister, or lump in 51.17 per cent. of the cases. There was a history of injury in 23.82 per cent. of the cases; burns represented 24.59 per cent. of the injuries, and roentgen-ray burns represented 20 per cent. of the burns. Data of interest are: 78.4 per cent. of all lesions occurred above the clavicle; 28.12 per cent. of the patients were treated with acid, paste or plaster before they entered the clinic; 26.95

per cent. were operated on at the clinic. Regional lymph nodes or salivary glands were not removed in 77.96 per cent. Of the 22.03 per cent. of the cases in which the regional lymph nodes or salivary glands were removed, metastasis was demonstrated in 61.53 per cent. The cervical lymph nodes were involved in 31.25 per cent., the submaxillary lymph nodes in 28.12 per cent., the parotid lymph nodes in 25 per cent., the parotid salivary gland in 25 per cent., and the axillary and inguinal lymph nodes each in 15.62 per cent. Of the patients operated on and traced, 51.77 per cent. are dead; 82.35 per cent. of the living patients have been free from the disease on an average of 7.44 years; 65.51 per cent. died of epithelioma. The actual operative mortality was 0.42 per cent. Patients who were treated with pastes, plaster, etc., before entering the clinic did not get such good total results as those who were not so treated, 57.14 per cent. in the former group and 61.11 per cent. in the latter; the total poor results were 40 per cent. in the former group and 30 per cent. in the latter. Of the patients with metastases, 10.52 per cent. are living. No patient with cervical lymph nodes or more than one group of any lymph nodes involved has been reported living. All the patients reported dead who had metastases died of epithelioma; 66.66 per cent. of the patients reported dead who did not have metastases died of epithelioma; 53.15 per cent. of the patients operated on in whom no regional lymph nodes or salivary glands were removed are living; 81.35 per cent. of these report good results; 54.76 per cent. of the patients reported dead in whom no regional lymph nodes or salivary glands were removed, died of epithelioma. The total good results for the patients with metastasis are 6.66 per cent.; for those without metastasis, 77.77 per cent.; and for those in whom no regional lymph nodes or salivary glands were removed, 66.33 per cent.

CORRECTION

In the abstract of the article on "An Experimental Study of the Latent Syphilitic as a Carrier," which appeared in the May issue of the *ARCHIVES*, on page 665, line 4 the word "semen" should be substituted for the word "serum."

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, April 19, 1921

ARTHUR W. STILLIANS, M.D., *in the Chair*

MORPHEA. Presented by DR. WAUGH for DR. OLIVER.

A girl, aged 10 years, had small annular lesions on the right popliteal space, left shoulder, arm and right thigh, which had been present one year. The lesions were the size of a small coin, slightly infiltrated, especially at the margins, and yellow or pinkish yellow. There was no subjective sensation.

DISCUSSION

DR. BAER was inclined to agree with the diagnosis of morphea, although he felt that it might be granuloma annulare. He recalled a similar case, of two years' duration, in which there were eight lesions; recent examination revealed the earlier lesions as scars only. The more recent lesions closely resembled those in the present case.

DR. SENEAR said that if it had not been for the large lesion he would have hesitated in agreeing with the diagnosis, but in his opinion the large lesion was typical of morphea.

DR. FOERSTER found a certain resemblance of the lesion to the fixed erythema, as seen after antipyrin ingestion, but was inclined to favor the diagnosis of granuloma annulare.

DR. PUSEY was not aware that morphea ever occurred in annular form. These lesions were perfect rings, and he was unable to accept the diagnosis of morphea. In his opinion there were only two possible diagnoses in this case: granuloma annulare and erythema elevatum diutinum, Crocker's term for what Dr. Pusey thought was the same disorder. He knew no reason why morphea and granuloma annulare should not coexist. He had recently had two cases of morphea coexisting with sarcoid.

DR. EISENSTAEDT recalled a similar case which he demonstrated before the Society last year. When the lesions healed they left morphea-like patches resembling the lesion in the present case.

DR. WAUGH stated that the lesion on the arm, when viewed in daylight, had a definite yellowish-white center with a lighter areola. In his opinion, the lesions resembled morphea more than granuloma annulare.

LUPUS ERYTHEMATOSUS OF THE LIP. Presented by DR. STILLIANS.

A German, aged 33 years, a mechanic, had had a scaly condition of the lower lip for two years. No lesions were found elsewhere, and there was no other disturbance of health. On the left side of the lower lip at the mucocutaneous juncture was a circinate lesion 1.5 cm. in diameter, with a slightly depressed, pale center and a dull, slightly yellowish-red border. On the right

side was a round lesion of the same dull red color. Both were covered by sparse adherent scales. On the inner side of the right cheek was a white macule about 0.75 cm. in diameter and not sharply defined.

DISCUSSION

DR. FOERSTER said it was unusual for the lesions of lupus erythematosus to be confined to the mucous membrane of the lip. He recalled a similar case shown before the Society in which typical lesions developed in the scalp several years later. In Dr. Stillians' case, the lesions on the vermilion border of the lip were typical of lupus erythematosus.

DR. WAUGH recalled a patient whom he had seen several years ago and presented to the Society, with lesions closely resembling those in the present case. At the time the case was presented, only one member of the Society suspected the presence of epithelioma, but later a biopsy was made and the tissue was found to be typical of squamous cell epithelioma.

DR. STILLIANS thought it rather strange that there were no scars present.

DR. SENEAR agreed with Dr. Foerster. He had examined the patient closely and had found areas of atrophy.

CASE FOR DIAGNOSIS. Presented by DR. H. R. FOERSTER.

A man, aged 49 years, a machine shop inspector, who was first seen on April 2, 1921, eighteen months before first noticed an eruption on the left leg, which increased to its present extent in about four months, and involved all of the right leg in the past six months. In the three years preceding the eruption he had received fifteen injections a year of a serum for the relief of hay-fever, the last injection in July, 1919. There had been no other medication. About six weeks ago phlebitis of the left thigh developed with spontaneous pointing and discharge, after three weeks, of pus and blood from an opening in the lower inner third of the thigh. The lesions begin as deep-seated vesicles, without subjective sensations; after from seven to ten days they are elevated above the surface as thin-walled bullae and assume angular stellate, circular or arcuate shapes, and have clear or, later, hemorrhagic contents. When they are the size of a large pea they usually rupture as a result of friction, and a closely adherent, crustlike scale covers the entire lesion. When the scale is loosened, after ten days, the base beneath is seen to be round or angular, raised and stippled with tiny depressions, often containing milia. A striking feature is the sharp limitation of the eruption on the legs to just above the shoetops, and the entire absence of lesions in the area of garter pressure. Small groups of an abortive type of the same eruption have appeared within the past five months on the left shoulder, both forearms and right thigh.

Differential blood count of 400 cells showed: polymorphonuclears, 58 per cent.; large mononuclears, 18 per cent.; small mononuclears, 11 per cent.; eosinophils, 8 per cent.; transitionals, 5 per cent.; total white blood cells, 5,950.

Physical examination was negative; the urine was normal, and a neurologic examination was likewise negative. A report on the pathologic histology will be made later. The diagnosis of lichen ruber pemphigoides and of an unusual form of dermatitis herpetiformis were under consideration.

DISCUSSION

DR. LIEBERTHAL was unable to make a diagnosis without further study. He asked about the appearance of the lesions and how the present lesion developed.

DR. FOERSTER replied that the lesions begin as deep vesicles and are never pustular. The fluid from the bullae with clear contents showed polymorphonuclear leukocytes and a few eosinophils.

DR. WAUGH considered dermatitis herpetiformis and mycosis fungoides. The lesions on the body strongly suggested the first disorder, but he had never seen dermatitis herpetiformis with lesions like those on the legs of this patient. The lesions on the legs, he thought, suggested those of mycosis fungoides. They had a tendency to circinate and annular arrangement and were definitely infiltrated.

DR. BAER did not wish to venture a diagnosis of the lesions on the legs, but those of the arms and back he thought resembled those of dermatitis herpetiformis.

DR. SENEAR thought the lesions on the body suggested dermatitis herpetiformis. Those on the legs were annular and in some places linear and resembled those of lichen planus, but the sharp demarcation at the garter line he thought would not occur in lichen planus, as the depression was probably due to vascular disturbance.

DR. PUSEY said the lesions on the legs suggested impetigo herpetiformis despite the fact that the patient was a man.

DR. O. H. FOERSTER thought the case might prove to be one of dermatitis herpetiformis, and was inclined to agree with Dr. Pusey as it presented features allying it with the more serious forms of bullous disease.

BROMID ERUPTION. Presented by DR. STILLIANS.

An American woman, aged 42 years, had had an eruption which had been diagnosed as blastomycosis of the right leg by Drs. Hyde and Montgomery in 1908. This condition was cleared up by a few weeks of treatment. A second eruption appeared in 1919 and again was cleared up after about six weeks of treatment. The present attack began in January, 1921. The patient had taken small doses of bromid for epilepsy for about twenty years.

At the time of presentation there was a thin scar involving nearly the whole anterior surface of the right leg and a little less of the posterior surface. At its upper border and in places within it were many areas of honeycomb appearance from which pus oozed, and a few beginning pustules were present. Some of these patches were slightly raised; others were level with the skin. At about the middle of the left shin were two small lesions similar to these.

DISCUSSION

DR. SENEAR thought the lesions on the legs were blastomycosis lesions.

DR. FOERSTER was inclined to believe that the lesion was one of fungating tuberculosis.

DR. STILLIANS regretted that he had as yet made no microscopic examination for blastomycosis. The patient had been taking bromids daily for a long period. The Wassermann reaction was negative; there had been no pustules for a long time until recently.

HYDROA VACCINIFORME. Presented by DR. SENEAR.

A man, aged 31 years, whose disorder was of seventeen years' duration, at the beginning of his trouble had lesions on the face, arms and cornea. He was treated by Dr. Hyde, who was able to prevent the development of further lesions on the cornea, but the patient still shows corneal scars which interfere considerably with vision. The condition is aggravated by sunlight and also by hot and very cold weather.

Examination showed numerous pitted scars in the cheeks, pitted scars in the cornea and some active vesicular lesions on the ear.

DISCUSSION

DR. PUSEY thought the case was interesting because of the rarity of the corneal involvement.

DR. SENEAR said the case was described in the seventh edition, 1904, of Dr. Hyde's textbook, and so far as he was able to find, there was no similar case.

A CASE FOR DIAGNOSIS. Presented by DRs. STILLIANS and CORCORAN.

An infant, aged 6 weeks, with bluish, deeply seated pigmentation over the sacrum and buttocks which had been present since birth, on the posterior surface of the left thigh had a bluish black oval macule about 4 by 3 cm., surrounded by a lighter bluish gray border 2 cm. wide. In the sacral and lower lumbar regions were irregularly shaped pigmented areas brownish in color, not sharply defined or deeply pigmented.

DISCUSSION

DR. PUSEY thought the eruption was probably a nevus.

DR. EISENSTAEDT believed it could be placed in the group of nevi. He did not consider it a Mongolian spot.

DR. BAER thought it belonged in the nevus group.

DR. CORCORAN said that in the extensive experience of Dr. DeLee no similar case had been encountered. The possibility of its being a Mongolian spot had been considered but rejected.

TUBERCULOSIS VERRUCOSA CUTIS WITH LICHEN SCROFULOSORUM. Presented by DR. STILLIANS.

A boy was shown at the January meeting of the Chicago Dermatological Society, and his case is reported in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY*, May, 1921, p. 688.

At that time the diagnosis of tuberculosis verrucosa cutis was called into question. At the present time the lesions on the leg showed some improvement, but there had been a recurrence of the lichen scrofulosorum on the body.

DISCUSSION

DR. EISENSTAEDT was satisfied that it was tuberculosis verrucosa cutis on the leg and that the eruption on the body was lichen scrofulosorum.

DR. TUCKER was inclined to believe that the case was one of ichthyosis.

DR. LIEBERTHAL at first thought of tuberculosis verrucosa cutis. He did not think that the papules on the body were those of lichen scrofulosorum

because of the character of the desquamation. The lesions in this case were follicular hyperkeratoses and those on the foot and leg were undoubtedly nevi.

DR. BAER was satisfied that the lesions on the leg were nevi. Those on the body he thought were too prominent for lichen scrofulosorum; they were obviously follicular keratoses resembling keratosis pilaris.

DR. FOERSTER thought the case was one of nevus associated with ichthyosis.

- DR. PUSEY agreed with Dr. Lieberthal. He believed it was a linear nevus on the legs and keratosis pilaris on the body.

DR. STILLIANS agreed that the lesion on the foot resembled a nevus but elsewhere on the leg the lesions were not linear and consisted of erosions covered by crusts. The eruption on the body underwent remissions and exacerbations, and in the interim the skin was clear in appearance. A biopsy was made before the patient was shown in January, but the excision was not sufficiently deep and it was without value. A skiagraph of the chest was negative.

DR. PUSEY said that a linear nevus need not necessarily be hyperkeratotic. In this case the hyperkeratotic mass probably was knocked off from time to time, and the red nodules had the appearance of tuberculosis verrucosa cutis.

MYXOSARCOMA. Presented by DR. STILLIANS.

A man, aged 58 years, in 1905 was shot through the lower portion of the right leg. The bullet entered the outer upper thigh and came out just below the knee on the inner side. The external popliteal nerve was sutured by Dr. J. B. Murphy. A lump, which gradually became larger and was excised in 1911, appeared at the site of the escape of the bullet. Since that time it had recurred, gradually increasing in size until last year, when it had grown more rapidly. At times there was stinging pain, and at all times it had been sensitive to touch.

On the inner side of the lower part of the right leg, just below the knee, was a soft, doughy swelling, 4 cm. in diameter and about 1 cm. high, which was not tender. It was freely movable with the skin and had no connection with the bones; it was covered with normal skin. Just above this and connected with it was a scar beneath which several hard nodules could be felt. These were adherent and only slightly tender.

DISCUSSION

DR. BAER suspected sarcoma.

DR. SENEAR was inclined to agree with Dr. Baer.

DR. STILLIANS said that during the operation in 1905 microscopic examination had been made and a diagnosis of myxosarcoma had been placed on the record. No biopsy had been made since that time.

HEMANGIOMA OF THE LIP. Presented by DR. FINNERUD.

An infant, aged 7 weeks, had a lesion on the vermilion border of the left side of the lower lip which had been present since or shortly after birth and recently had become necrotic. Before coming under the observation of Dr. Finnerud the diagnosis of chancre had been made. There was no localized adenopathy and dark-field illumination revealed no spirochetes. The case was presented as a necrotic hemangioma with secondary infection.

DISCUSSION

DR. PUSEY thought the case was one of spontaneous breaking down of a hemangioma with secondary infection. He recalled seeing a child with lesions over the entire side of the face. The application of carbon dioxid snow in a few places resulted in the sloughing off of the entire angioma. The result was excellent. He believed this angioma was probably undergoing a spontaneous involution.

DR. FINNERUD said that the parents of the infant were sure that the lesion was becoming larger. It already extended into the mucous membrane of the lip. He wished to have the opinion of the members of the Society concerning the advisability of radium at the present stage.

DR. PUSEY said that if the lesion was extending to the mucous membrane, radium should be used at the earliest possible moment.

TWO CASES OF FAVUS OF THE SCALP IN THE SAME FAMILY.

Presented by DR. STILLIANS.

Two sisters, one a student aged 23 years, both American born, had had a disease of the scalp since childhood; three sisters of a family with five children were infected from a German servant girl. In spite of the long duration of the disorder only a few small scars were present in the younger of the two patients shown, and only the vertex was involved. About the borders of the scars were many scales and a few small, yellow granules in which the achorion was found microscopically.

In the married sister, aged 30 years, still less scarring was present and only a slight degree of scaling. The third sister was reported to have wholly recovered.

DISCUSSION

DR. PUSEY said he had been seeing many more cases of home-grown favus recently than in former years.

DR. EISENSTAEDT thought the striking thing in these two cases was the small amount of scarring.

DR. MITCHELL said he had recently seen two members of a family of six girls, all of whom were born in Holland, and all of whom were said to be infected. He had grown the achorion of Schönlein in these cases.

DR. LIEBERTHAL stated that in his experience it was not unusual to see small areas of alopecia in this country, which was probably due to the fact that patients in this country take much better care of their scalp than do those in Europe. In the treatment of favus he had obtained excellent results in a rather large series of cases with a combination of chrysarobin, pyrogalllic acid and ichthyol.

DR. PUSEY agreed with Dr. Lieberthal that the small areas of alopecia were probably due to the superior sanitary care given the scalp in these native born patients. In his own experience he had never seen a cure without either the use of the roentgen ray or radium therapy. He had obtained excellent results in ringworm of the scalp with radium.

DR. LIEBERTHAL thought he had probably been the first to treat ringworm of the scalp by means of roentgen therapy. In 1901 he had treated ten cases without any untoward results.

GRANULOMA INGUINALE TROPICUM. Presented by DR. STILLIANS.

The patient was a negro, aged 28 years, who was demonstrated before the Society in 1920. He had been treated by curettage followed by cauterization with phenol, with partial healing, but the disease had always recurred promptly when he returned to work, and the ulcers about the arms were difficult to curet. With the use of a 1 per cent. solution of tartar emetic given intravenously he had made a more rapid improvement than ever before, and at the time of presentation seemed well. Many thick white scars were present in both groins, on the perineum and on the penis, marking the sites of the former ulcers.

DISCUSSION

DR. PUSEY thought the result was very interesting. He was inclined to believe that many cases of so-called granuloma inguinale tropicum in this country were nothing more than phagedenic chancroids, and before he accepted the diagnosis he would like to know the effect of tartar emetic on some of the old phagedenic chancroids in negroes. The condition was certainly not of great rarity in this country.

DR. STILLIANS believed that treatment with intravenous injections of tartar emetic should be tried in cases of chancroid before a cure by this method could be held to have diagnostic value.

DERMATITIS NODULARIS NECROTICA. Presented by DRs. STILLIANS and FINK.

The patient was the man shown at the March meeting of the Society. Since that time he had been in the hospital on ordinary hospital diet and care. Great improvement had resulted without any definite treatment. Two subcutaneous tuberculin tests had been given without reaction.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

A man, aged 42 years, had had an itching papular eruption for nearly twenty years. Recently he had gone to Hot Springs, where he had received intensive treatment with resulting severe stomatitis. On the inner surface of the right cheek was a slough 3 by 2 cm. in diameter, and many of the teeth were loose; the gums were swollen and spongy and pus oozed from between them and the teeth. On the extensor surface of the arms and forearms were many papules capped by blood crusts. These were also present on the trunk, but were less numerous. The skin of the extensor surfaces was not markedly thickened. The patient stated that the eruption used to be greater on the legs. The inguinal and axillary glands were palpable, but not large.

DISCUSSION

DR. PUSEY thought the papular eruption resembled acne urticata.

DR. EISENSTAEDT said the lesions suggested prurigo.

DR. TUCKER said he had thought of prurigo, but the absence of lesions on the legs and arms made him hesitate to accept that diagnosis. He was inclined to agree with Dr. Pusey.

DR. LIEBERTHAL believed the case was one of dermatitis herpetiformis of the nodular type. It is well known that prurigo improves in the summer.

DR. SENEAR had not thought of acne urticata or prurigo until they were

mentioned. He was inclined to favor the diagnosis of dermatitis herpetiformis because of the recurrence, the pigmentation and the pruritus.

DR. PUSEY said the case did not fit in with prurigo of either the mild or severe type as described by Hebra. In prurigo the lower half of the body is the portion chiefly involved, and even in the mild type there are shotty papules. The inflammatory element is due in large part to scratching. The lesions in this case occurred in the "V" area of the back, which did not agree with the disorder as described by Hebra.

DR. FOERSTER said that one could easily eliminate prurigo of Hebra because of the absence of infiltration which in that disorder increases from above downward. In this case the lesions have soft centers and are exudative in type, more nearly like lichen urticatus.

DR. STILLIANS was inclined to make the diagnosis of lichen urticatus, but believed that there are cases of mild prurigo in which there are lesions on the upper part of the body.

DR. EISENSTAEDT asked how frequently one sees lichen urticatus persist after puberty.

FORDYCE'S DISEASE OF THE UPPER LIP. Presented by DR. STILLIANS.

An American, aged 19 years, a flute player, last October obtained a new mouthpiece for his flute. About the middle of November the upper lip became chapped, and he bit off the scales that formed. A crust then formed at the center of the upper lip; it had dropped off and reformed several times each week since then. The pain was slight, and was present only when the crust separated or was torn loose.

The upper lip was covered along its entire length by a band, averaging 0.5 cm. in width, of closely set, yellowish-white papules. At the center of this band was an adherent, thin crust, covering an erosion; outside this erosion was a border of the small white papules. At the time of demonstration the center area had apparently healed as the result of radium therapy.

DISCUSSION

DR. PUSEY thought it was unusual to have so many lesions on the mucous membrane of the lip and so few on the buccal mucous membrane.

LUPUS ERYTHEMATOSUS. Presented by DRs. ORMSBY and MITCHELL.

A man, aged 36 years, had had a dermatitis of the urticarial type on the face, arms and legs for the past three months. He had been under observation since Feb. 10, 1921. During that time the dermatitis on the face had resisted all ordinary soothing treatment, including radiotherapy. Within the past month the lesions on the face had undergone changes which left no doubt as to the diagnosis.

The lesions at the time of presentation were well defined, superficial reddened areas with some telangiectasia. They occupied the greater part of both cheeks and were symmetrical.

DISCUSSION

DR. MITCHELL considered the case interesting as the patient had, when first seen, what appeared to be an ordinary dermatitis on the cheeks and various parts of the body. The lesions on the body had completely cleared, and the urticarial element had disappeared. While under observation they had been able to observe the transformation of a dermatitis into definite and typical lesions of lupus erythematosus.

NEW YORK DERMATOLOGICAL SOCIETY

*Regular Meeting, April 26, 1921*JAMES McF. WINFIELD, M.D., *President*

ACANTHOSIS NIGRICANS. Presented by DR. GEORGE HENRY FOX.

S. C., a boy, aged 13, five years ago had pigmentation of the axillae which developed in areas about the lips, neck and arms. The affected skin assumed a dull bluish hue and became slightly thickened, with deepening of the natural lines. This condition gradually increased, but only within the past month had verrucous patches developed. The oral mucosa was slightly affected, and the boy appeared to be in good health. Since first seen in consultation with Dr. LeVine of Patterson, the eruption had undergone considerable change. The scalp, which had been little if at all affected, was now covered with flat warty nodules and scales suggesting psoriasis. The various patches had peeled as the result of treatment, leaving a pinkish, unpigmented surface.

DISCUSSION

DR. HIGHMAN said that as presented the eruption did not resemble acanthosis nigricans; also the age and sex of the patient were against that diagnosis. The appearance of the eruption was altogether different from that described by Dr. Fox as first seen. It was a thickened, scaling eruption suggesting an atypical psoriasis, or it might be an atypical Darier's disease, or possibly an atypical hyperkeratotic tinea. The boy had had pigeons as pets. A histologic study of the lesions should be made. The pigmentation preceded the eruption by five years, and was followed by ptomaine poisoning. Possibly he might have had an arsenical eruption for five years, etc.; there was no indication of any visceral involvement.

DR. HOWARD FOX said that the eruption had changed greatly since he had seen it two weeks previously. At that time there was a roughened, acanthotic and pigmented appearance of the axillae and cubital spaces. There now seemed to be a secondary eruption which masked the original one and suggested a possible psoriasis. He could not agree with Dr. Highman about the importance of age and sex in a disease which was so extremely rare as acanthosis nigricans.

DR. WISE regarded the case as an example of erythroderma ichthyosiforme. Some years ago Drs. MacKee and Rosen published a comprehensive paper on this subject in the *Journal of Cutaneous Diseases*. Some of the cases described in their paper corresponded in most details with the one presented. One of the patients therein described was observed by the speaker when he was an intern at the Skin and Cancer Hospital. In this patient, a young girl, the eruption was at first considered to be an acanthosis nigricans, but later the correct diagnosis of ichthyosiform erythroderma was established.

DR. LEVINE said the patient had recently presented a very different appearance. The boy had always been healthy and athletic. The pigmentation had existed for five years, and only during the past few weeks had the verrucous lesions on the chest appeared and spread to the arms and legs. When Dr. Fox suggested acanthosis nigricans, the textbook descriptions were studied and the condition seemed to correspond completely; but since that time the skin had changed in color where peeling of the verrucous patches had taken place.

DR. G. H. FOX said that when he first saw the case the dark axillary areas recalled a girl seen at the Skin and Cancer Hospital, a case which was for some time called *acanthosis nigricans* but proved to be congenital ichthyosiform erythroderma. As Dr. Wise had suggested, this case might present the same condition and not be true *acanthosis nigricans*, but it certainly bore a close resemblance to the description of the few cases which had been reported as such.

CASE FOR DIAGNOSIS. Presented by DR. BECHET.

Miss E. E., aged 21, born in the United States, stated that she first noted the eruption twelve years previously. When first seen in April, 1912, the lesions exhibited very much the same appearance as at the time of presentation. There was considerable scarring from previous applications of some cauterizing agent. Several of the lesions were eradicated at that time by means of electrolysis. The patient then disappeared from observation until a few days previous to presentation, an interval of nine years having elapsed. In that period of time there had been little, if any, change in either the number or appearance of the lesions. They were unilateral and were located on the right side of the neck, below the ramus of the jaw. They were polygonal in outline, of a brownish red color, and noninflammatory. There was no itching or other subjective symptoms. The patient's health was excellent, and her family history was negative.

DISCUSSION

DR. WISE said he could not make a diagnosis, but for the sake of discussion suggested the possibility of *pseudoxanthoma elasticum*.

DR. HIGHMAN thought it might be *xanthelasma*, which sometimes occurred in the platysma, or *pseudoxanthoma elasticum*. It seemed too elevated for the latter. On closing the eyes, one could not tell whether one was passing over the lesions or over the skin. The only way to reach a diagnosis would be by histologic examination.

DR. BECHET stated that he would try to gain the patient's consent to a biopsy and report the result at a future meeting of the Society.

LICHEN PLANUS HYPERTROPHICUS. Presented by DR. HOWARD FOX.

M. V., aged 33, born in Italy, a woodworker by trade, first noticed the eruption eight years previously. He presented two oval, infiltrated, fairly sharply circumscribed patches on the lower third of the antero-external aspect of the right leg. The patches were about 2 inches in their long axis, verrucous to the touch, and dry and slightly scaly. There were bright red borders surrounding the dark purplish central portion. Another patch adjacent to the present ones had disappeared spontaneously without leaving any trace. There were no other cutaneous lesions. One patch was being treated by radium and another by roentgen-ray for comparison.

VESICULAR AND BULLOUS ERUPTION. Presented by DR. WHITEHOUSE.

Harry W., aged 14, had diphtheria ten years ago and received antitoxin, after which he was confined to the Willard Parker Hospital for six months; the diphtheria was followed by scarlet fever, noma and measles. He was said to have had measles and scarlet fever twice. He had a discharging sinus when he left the hospital, and was a long time regaining his health. When he con-

valesced, he put on weight rapidly, and during the past seven years gained steadily until he weighed 150 pounds, as presented. The eruption presented had appeared every spring for the past seven years, affecting the palmar surfaces and sides of all the fingers; the palms were unaffected, and the feet were never involved. The hands perspired excessively, and the eruption was less severe in late cold springs than in early warm springs. It always disappeared in two or three weeks, causing no trouble during the summer. The eruption was vesicular and bullous in type, simulating very much dermatitis venenata. One bulla was an inch long, and another was as large as a marble. The boy was unusually bright, but was gaining weight rapidly; incidentally, there had been complete arrest in the development of his sexual organs.

The case was presented as a vesicular and bullous scarring eruption simulating pompholyx or dyshidrosis—the latter diagnosis had been made—but with features suggesting possible endocrine association. It suggested to the speaker that the thymus might still be functioning, holding the gonads in abeyance, and the question arose as to whether the antioxin or the severe infections he suffered ten years previously entered into etiologic relationship to the subsequent developments.

DISCUSSION

DR. LANE said that on general principles, before making any other diagnosis of the eruption on the hand, it would be necessary to exclude ringworm. That diagnosis seemed probable.

DR. WISE did not think the vesicular lesions had anything to do with the boy's endocrine glands, and agreed with Dr. Lane that ringworm should be excluded.

DR. WHITEHOUSE said he had been interested in the possibility of the connection of the condition with some endocrine gland disturbance, and that he would probably put the patient in the hands of some one who would work up that side of the case. It might be that the eruption was a recurring type of dyshidrosis and not connected with the other condition.

ARSENICAL KERATOSIS. Presented by DR. BECHET.

Miss E. B., aged 21, born in the United States, stated that she had had chorea seven years previously. The disease was severe, and ran a prolonged course. For its relief, she was given Fowler's solution in doses varying from 5 to 20 drops three times a day, for months at a time. Arsenical medication was continued, with varying intervals of rest, for four and a half years. The hyperkeratosis first began to appear five years previously, and two years after beginning the arsenical treatment. She had a marked keratosis of the palms and soles, so severe as to be almost horny in spots. Warty excrescences, superimposed on the keratotic lesions, were observed on the palms. The eruption was extensive.

TELANGIECTASIS FOLLOWING ROENTGEN-RAY TREATMENT. Presented by DR. TRIMBLE.

A young woman, aged 23, who had suffered from a rather severe acne for about ten years, for the past year had been receiving roentgen-ray treatment. According to her statements, it was seemingly given in the modern way, although she asserted that she had had quite a number of exposures over a period of about one year. Both sides of her face were covered with telangiectases which produced the appearance of a vascular nevus.

DISCUSSION

DR. WISE said that for about eight years he had been using roentgen-ray treatment for acne in properly measured doses, and had never seen any untoward results. He considered roentgenotherapy the treatment par excellence for acne vulgaris.

DR. BECHET told of an interesting case seen in private practice before the massive dose method had been devised. The patient had received only two short roentgen-ray exposures directed on the chin, for the relief of a moderate acne. These exposures were made by a most careful and experienced operator. A marked atrophy of the skin resulted. There was no telangiectasia. The patient, a woman, aged 35, had the wrinkled chin of a woman of 80. The condition was most disfiguring, as the rest of the face was absolutely smooth. The acne was still present.

DR. HOWARD FOX said that when he advocated the use of the roentgen ray in the treatment of acne or other skin diseases, he explained that only accurately measured doses should be used.

CIRCINATE SYPHILID IN A YOUNG WHITE WOMAN. Presented by
DR. WISE for DR. FORDYCE.

B. B., aged 17, unmarried, a telephone operator, presented herself at the Vanderbilt clinic with a circinate, scalloped and seriginous eruption, especially on the cheeks and forehead, of a few days' duration. Some of the annular lesions were the size of a half dollar and presented quarter-dollar sized lesions within the larger ones. She had mucous patches of the fauces, and a generalized adenopathy. She received arsphenamin immediately, causing the lesions to fade rapidly.

CASE FOR DIAGNOSIS (PREVIOUSLY PRESENTED). Presented by
DR. CLARK.

N. P., aged 38, a clerk, had a negative family history; his general health had always been good. This patient had already been presented at the April meeting of the Section, but although a biopsy had been made the diagnosis was still in doubt.

The biopsy showed a deep-seated lesion composed of aggregations of lymphocytes with groups of endothelial cells. There was also infiltration of the superficial derma, showing many polymorphonuclears. Ziehl's stain was negative for acid-fast bacilli.

DISCUSSION

DR. HIGHMAN said it was hard to size up the case. It suggested lupus pernio of Leloir, or perhaps atypical disseminate lupus erythematosus. That was all he could think of. The case would require prolonged observation and clinical study. Lupus pernio of Leloir was considered tuberculous, but clinically resembled lupus erythematosus.

DR. WINFIELD was inclined to agree with Dr. Highman.

DR. CLARK said that a tentative diagnosis made by the pathologist was possible sarcoid, but he had no suggestions to make.

PIGMENTATION OF THE BUTTOCKS. Presented by DR. HOWARD FOX.

D. G., an ex-soldier, aged 23, born in Ireland, about three months ago first noticed an eruption covering the entire surface of both buttocks, which had not occasioned any subjective symptoms. It was a reticulated, dull-colored,

brownish macular eruption, with a suggestion of a violaceous tinge. There was slight branny scaling. Before the eruption appeared, he had received roentgen-ray treatment for possible disease of the genito-urinary tract, and later for possible disease of the coccyx and sacrum. The radiograms had, however, been taken anteriorly and laterally, no exposure having been made posteriorly.

DISCUSSION

DR. WISE believed the diagnosis to be erythema ab igne. He did not think the disease had anything to do with the roentgen rays.

NAEVUS ANAEMICUS. Presented by DR. HOWARD FOX.

H. S., an ex-soldier, aged 22, a clerk, presented a patch on the left side of the chest, $1\frac{1}{2}$ inches in diameter, made up of eight separate smaller areas of various shapes and sizes. They were whitish, smooth, of normal consistency, and gave rise to no subjective symptoms. The patch had existed since birth, and was incidentally discovered when he applied for treatment of another condition.

SEBORRHEIC ECZEMA. Presented by DR. WISE for DR. FORDYCE.

A. G., aged 68, a white American, presented himself at the Vanderbilt clinic with a generalized eruption of five weeks' duration. The eruption was intensely red and exhibited an associated exfoliation. The exfoliation was especially marked on the palms, thighs, and backs of the legs, where the condition resembled an exfoliating erythroderma. The inflammatory condition with scaling of the scalp, face and back of the neck suggested eczema. The patient had a marked general adenitis. The Wassermann reaction was negative.

The case was presented for further suggestions as to the diagnosis. The biopsy confirmed the diagnosis of seborrheic eczema.

DISCUSSION

DR. HIGHMAN said that he could not make any microscopic diagnosis. He thought it was either a seborrheic or psoriasiform condition. There was no suggestion of leukemia. When he saw the patient this evening and observed the general adenopathy, he had suggested that the condition belonged in the leukemic group. The case should be studied from that point of view especially as to hematology.

DR. WHITEHOUSE thought the lesions looked like seborrheic eczema. The adenitis might be independent of the eruption. The condition of the palms was not inconsistent with the diagnosis of seborrheic eczema.

DR. HOWARD FOX agreed with Dr. Whitehouse.

DR. BECHET thought that he had discovered some slight infiltration in the lesions on the sides of the buttocks and over the thighs. This, and the general appearance of the lesions, suggested the possibility of premycosis.

LUPUS ERYTHEMATOSUS (?). Presented by DR. WISE for DR. FORDYCE.

W. McC., aged 27, white, an American and an elevator constructor, presented himself with an eruption confined to the face, back of the neck and right upper arm of three years' duration, and with a history of the total disappearance at times of all the lesions. The eruption on the face and back of the neck suggested a dermatitis venenata, but the condition of the arm was different. Here the eruption was well defined, erythematous, infiltrated, slightly lichenified and showed slight atrophy. It was somewhat pruritic.

DISCUSSION

DR. HIGHMAN said that clinically the case resembled lupus erythematosus, and there seemed to be enough in the histologic picture to support that diagnosis. The picture under the microscope was not typical, but neither was it against that diagnosis. No satisfactory histologic diagnosis was reached.

Several of the other members concurred in the diagnosis.

ALOPECIA AREATA TREATED WITH QUARTZ LAMPS. Presented by
DR. HOWARD FOX.

P. R., aged 26, a laborer, born in Ireland, applied for treatment in July, 1920, for an extensive alopecia areata of two years' duration. He then presented two small tufts of thick hair on the vertex and a fringe of thick hair in the occipital region. Over the rest of the scalp new downy hair had made its appearance two months previously. The vertex of the scalp was given eleven weekly exposures to the Alpine sun lamp, at the end of which time he discontinued treatment. He now presented a vigorous growth of thick dark hair over the entire vertex, the only part of the scalp that had been treated. In addition, there was some increase in the growth of hair at the borders of the scalp (not treated). The vigorous growth of hair had appeared about three weeks after the cessation of treatment.

DISCUSSION

DR. BECHET said that he had seen some good results with the Alpine sun lamp in alopecia areata. According to his experience, the hair returned more rapidly and the returning hair was less apt to be white through the use of the lamp than by any other means of treatment.

DR. LANE said that there was a good growth of hair over the area where the light had been applied. He would have more confidence in the efficacy of the treatment if some cases could be shown in which there was good growth of hair on the bald places which had not responded to other methods of treatment. The appearance of the hair in this case was quite usual even in untreated cases—good growth of hair, alternating with bald areas. In other words, he had little confidence in any of the methods of treating alopecia areata; mild stimulation of one sort was as good as another and perhaps not much better than none at all.

DR. HOWARD FOX felt that it was generally agreed that treatment by local stimulation was of value, recognizing, of course, that the disease was usually self limited. He considered the quartz lamps a convenient means of applying local stimulation. The present case was not shown as a brilliant result, but one in which the hair had grown on the treated area.

PERSISTENT PIGMENTATION FOLLOWING VARIOLA. Presented by
DR. HOWARD FOX.

The patient was a young Italian immigrant from the hospital at Ellis Island. He had suffered from smallpox ten months previously, presenting typical pitted scars of the face. He also presented a considerable number of small yellowish-brown pigmented macules, most numerous on the face, trunk and backs of the wrists and hands. The pigmentation was less conspicuous on the face, where the scarring was most apparent. Some of the pigmented lesions on the trunk and hands showed slight scarring.

DISCUSSION

DR. WINFIELD said he had never seen a case of pigmentation that lasted as long as this case had; usually pigmentation disappeared within three months after recovery from the disease. There was apt to be more pigmentation when the pustules were superficial.

DR. WHITEHOUSE remarked that the young man had a very dark skin, which might partly account for the continuance of the pigmentation.

DIFFUSE TELANGIECTASIA OF THE TRUNK. Presented by Dr. WISE for Dr. FORDYCE.

A. R., aged 35, born in Russia but a resident in the United States for nineteen years, was a clothier. He presented himself at the Vanderbilt clinic, complaining of hives, and when examined, areas of telangiectasia were noticed on his arms and trunk. This vascular dilatation of the trunk and arms was recognized as the telangiectasia mentioned by Stokes in an article written a few years ago. The patient was unaware of its presence or duration and, so far as he knew, none of his family had presented a similar condition. The Wassermann reaction was negative.

LICHENOID SCLERODERMA. Presented by Dr. WISE for Dr. McCafferty.

A. M., aged 39, a married woman, born in the United States, had presented herself with an eruption confined to the chest, right side of the neck and right portion of the back just below the angle of the scapula. The eruption on the chest had been present for six years, and as presented exhibited an atrophic scar measuring one inch in length by one-eighth inch in width. The eruption on the neck was of four years' duration and consisted of several atrophic, white scars the size of a split pea surrounded by a slight erythema. The lesion on the back was of six months' duration and was the size of a silver dollar. It was covered by a crust one-eighth inch in thickness, which when detached presented numerous cone-shaped projections which had fitted into corresponding depressions in the lesion. The lesion itself, without the scab, presented a pinkish-white color which suggested atrophy, and contained many large dilated follicles. The periphery showed the suggestion of a pearly border surrounded by a narrow zone of erythema. The lesion was completely excised, but the pathologic report had not been received.

DISCUSSION

DR. LANE was not sure about the condition, but thought that the lesion on the back should be cut out entirely. He had never seen such a scab in lupus erythematosus. It seemed quite probable, as had already been suggested, that it might be an epithelioma developing on a pre-existing lesion.

DR. WINFIELD cited the case of a woman doctor seen some years ago, who had a small lesion caused by pressure of a corset bone, which was diagnosed as lupus erythematosus. The spot gradually increased in size and changed in character. When the patient came under observation, the lesion was undoubtedly epithelioma. It had the exact appearance of the lesion in this case.

DR. CLARK said that he received the impression of a possible lupus erythematosus from the old condition—the lesions on the outer edge of the main lesion on the scapula looking like lupus erythematosus with slight atrophy.

The crust that was removed was like that one would find in such a lesion. It did not seem to him like an epithelioma. It appeared to be inflammatory and not hard along the edges.

DR. HIGHMAN agreed that the lesion on the upper part of the neck was probably a lichenoid scleroderma, but thought that the one over the scapula might be a basal cell epithelioma with an amazing type of scale or crust. He would make that diagnosis tentatively from the clinical standpoint.

Book Review

A PRACTICAL TREATISE ON DISEASES OF THE SKIN FOR THE USE OF STUDENTS AND PRACTITIONERS. By OLIVER S. ORMSBY, M.D., Professor and Head of the Department of Skin and Venereal Diseases, Rush Medical College (in affiliation with the University of Chicago); Dermatologist to the Presbyterian, St. Anthony's and West Suburban Hospitals, and the Home for Destitute Crippled Children; Consulting Dermatologist to the Orphan Asylum of the City of Chicago; Member of the American Dermatological Association and of the Congress of American Physicians and Surgeons; Corresponding Member of the Section of Dermatology of the Royal Society of Medicine, London. Second Edition, Thoroughly Revised. Pp. 1166, illustrated with 445 Engravings and 4 Plates in Colors and Monochrome. Philadelphia and New York: Lea & Febiger, 1921.

The second edition of this work incorporates within its pages a considerable amount of material which is new. About 400 pages have been revised and rewritten and a description of fifteen new diseases has been added. The references to the literature have, so far as it is possible, been brought up to date, the author having made a fruitful effort to include references to selected papers and monographs containing full bibliographies to the date of publication. To one who is accustomed to grapple with the task of looking up references, the value of such a procedure will be obvious, for a great deal of time and toil may be saved by getting hold of a single up-to-date bibliography, instead of wading through a maze of references which antedate the more recent publications. More space may thus be utilized for the text itself, to say nothing of illustrations, which indisputably are helpful to the beginner.

In going over the pages, the reviewer tried to imagine himself in the position of the novice—the medical student—who knows nothing of dermatology, but who must, *nolens volens*, learn at least a little of it. In assuming the average young medical student's mental attitude toward the subject, it is not at all difficult to invest oneself with a critical, not to say a meticulous, state of mind. The student approaches the subject with more or less reluctance—too often with distinct distaste—fearing that it is too obscure and too involved for him to grasp; that, after all, dermatology is only a minor subject in the curriculum, and that a little intensive cramming for the inevitable examination will suffice to bring about the desired results.

The value of Ormsby's book, it seems to the reviewer, lies in large measure, in the introductory matter which the student is urged to read and to absorb, before he takes up the study of the many—to him confusing—details which follow; he begins at the bottom of the ladder, obtaining the necessary groundwork for the proper understanding of the succeeding chapters. The chapters on general symptomatology, pathology, etiology, diagnosis and treatment are written with this object continually in mind; and they are easy to understand. They embrace a description of most of the useful modern diagnostic procedures, such as the Wassermann and Noguchi tests for syphilis, the tuberculin, von Pirquet and ophthalmo-tuberculin tests for tuberculosis, and so forth. The subject of general therapeutics takes up thirty-seven pages, dealing with internal and external remedies in common use, and including concise paragraphs on roentgen and radium therapy, phototherapy, electrolysis, fulguration, refrigeration and other dermatologic procedures.

In the description of the various disease entities, the author shows excellent judgment in apportioning to the important diseases the appropriate space which they deserve, and in confining himself to brief descriptions when dealing with the less important subjects. Frequently an author is likely to be carried away by his enthusiasm and interest over a relatively rare and unimportant malady which he may have investigated, devoting so many paragraphs to it that he soon finds himself cramped in his effort to mete out to the important and more common affections their full share of space. Eczema takes up thirty-seven pages, psoriasis twenty-one pages, tuberculosis and lupus erythematosus fifty pages and syphilis seventy-two pages. Many of the rare diseases and tropical dermatoses, however, are fully described. The chapter on trichophytosis is illuminating, embracing a description of many varieties of dermatophytes, with their pathology and bacteriology.

Here and there, the reviewer encountered paragraphs which might later be subjected to revision. For instance, Ormsby says that in the treatment of portwine marks, "liquid air, carbon dioxid snow and radium have given the best results." With some of us, it is the pressure treatment with the Kromayer light which has been found to be by far the most valuable method for eradicating these nevi. For the elevated capillary nevus, radium is without doubt the best remedy. The type of erythema perstans mentioned on page 138, was, subsequent to Ormsby's completion of his manuscript, found to be due in all cases to the ingestion of phenolphthalein, so that it might henceforth be included under the heading of drug rashes.

Some of the older illustrations have been replaced by better ones, and a large number of new ones have been added. The book is not too heavy, is well bound, and the paper and type are beyond criticism.

One turns from the book with a profound respect, not only for the author's extensive knowledge of the subject as a whole, but also for his excellent judgment as to what should be included in a textbook for the student and practitioner.

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Archives of Dermatology and Syphilology

VOLUME 4

AUGUST, 1921

NUMBER 2

SUBACUTE MALIGNANT PEMPHIGUS WITH EXTENSIVE BULLAE*

(Pemphigus Subaigu malin à Bulles Extensives, Brocq)

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INTRODUCTION

Brocq, whose studies have done much to bring comparative order out of the chaos which existed in the bullous dermatoses, has recently called attention to a group of cases of pemphigus hitherto not usually separately described.¹ He has given the name subacute malignant pemphigus with extensive bullae to the condition, which he describes as closely resembling acute febrile pemphigus, but which is differentiated from it by a characteristic clinical syndrome.

While Brocq's classification of pemphigus is the one now usually accepted, there is still enough variation in the usage of the term to warrant summarizing the conditions included under it, before describing the new syndrome, and locating it in the general scheme.

Under pemphigus Brocq includes acute febrile pemphigus (pemphigus aigu fébrile grave), pemphigus foliaceus, pemphigus vegetans and chronic pemphigus (or true pemphigus). He subdivides the last into two varieties, malignant chronic pemphigus (pemphigus chronique vrai grave), and benign chronic pemphigus (pemphigus chronique vrai bénin), thus admitting into this group the few cases of apparently true pemphigus which terminate in recovery.

We are not here concerned with pemphigus foliaceus or pemphigus vegetans.

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Acute febrile pemphigus is an apparently infectious disease characterized by a sudden onset and intense febrile reaction, an eruption consisting solely of serous or hemorrhagic bullae and by a fatal termination within one to three weeks, recovery being rare. It is seen almost entirely in butchers and in those who handle cadavers of animals. It is probably an acute infectious disease.

Chronic pemphigus is usually of insidious onset, is characterized by a widespread monomorphous bullous eruption which arises rapidly without evidence of inflammation of the skin, which is attended with little or no pain or pruritus, which affects the whole body and in which the bullae are reproduced in successive crops. The mucous membranes are frequently affected early in the disease. There is a fatal termination within a few months to a year, but there are frequently intermissions in the progress of the disease, with temporary improvement.

SUBACUTE MALIGNANT PEMPHIGUS

Brocq describes subacute malignant pemphigus as a syndrome presenting the general appearance of a severe infection without high temperature but with marked prostration of the patient who remains in bed without moving, immobilized by the severe pain which occurs on the surface of the excoriations whenever motion is attempted, speaking only with great difficulty on account of the lesions of the throat, of the soft palate, of all the buccal mucous membrane and that of the lips, lesions which are superficial but extremely painful.

In its evolution this syndrome is characterized by its frequent origin on the mucous membrane and in its objective appearance by the perfectly characteristic aspect of the cutaneous lesions which, on the site of the broken bullae, rapidly develop denuded, moist, sanguinolent surfaces which show no tendency to heal and which extend progressively at the edges with detachment of the horny layer of the skin.

This peripheral extension, simulating that of an extremely virulent impetigo, without tendency toward cicatrization in the center of the lesion, together with the gravity of the general condition in spite of only moderate fever and the suffering experienced by the patient, appear to him to establish a characteristic syndrome which gives this clinical picture an individual aspect, and which permits its immediate differentiation not only from dermatitis herpetiformis and dermatite polymorphe but also from all other bullous diseases. It also permits a bad prognosis. In the last twelve years Brocq has seen several such cases, six of them terminating in a relatively rapid death. There were two patients who either recovered or disappeared from observation greatly improved, but in these two cases the bleeding surfaces following the rupture of the bullae were not large, and the peripheral extension was slight.

Brocq's description of the syndrome just quoted is sufficiently detailed to obviate the necessity of summarizing the cases he reports.

We have recently had the opportunity of studying a patient who presented a typical picture of this syndrome.

History.—M. B., No. 78669, 69 years of age, was a widow born in Italy. She was admitted to the New Haven Hospital on Dec. 29, 1920, complaining of painful sores on her chest, abdomen and back. These had started six weeks



Fig. 1.—Early appearance of lesions.

before as small vesicles on her sides, back and neck, which had rapidly increased in size and number. She had had no previous illnesses of any consequence. She had had ten children, three of whom were alive and well, and seven had died between the ages of 5 months and 6 years.

Examination.—The physical examination revealed nothing of consequence except a slight soft systolic murmur at the aortic area and slightly sluggish pupils. She had no teeth. Blood examination on Dec. 30, 1920, showed hemoglobin 80 per cent, white blood corpuscles 22,600, polymorphonuclears 81 per

cent., small mononuclears 16 per cent., large mononuclears 3 per cent., eosinophils 0, basophils 0. A blood culture taken Dec. 31, 1920, showed no growth. A second culture taken Feb. 9, 1921, was also negative. Cultures from the bullae were not made because there was no possibility of obtaining uncontaminated material. The Wassermann reaction on Dec. 31, 1920, was negative with alcoholic antigen and + with cholesterinized antigen. The urine during her stay in the hospital was negative, except that an occasional specimen contained a faint trace of albumin. The temperature ranged between 98 and 102 F. and was usually about 100. Within the two weeks previous to her death it reached 103 once or twice. It was about 100 just before death.



Fig. 2.—Later appearance of lesions.

When the patient was admitted to the hospital her chest and back were covered with lesions varying in size from that of a silver dollar to that of the palm. These lesions were all covered with thick, partly dried, yellow crusts which had formed on the sites of previous bullae which had received no attention. Their appearance on the chest, where they were largest, resembled that of a severe neglected impetigo in a debilitated subject. On the back they more closely resembled the usual lesions of chronic pemphigus, as is shown in Figure 1. There were no lesions in the mouth. A few days after the crusts had been carefully removed the lesions presented smooth, red, moist denuded areas

which rapidly extended at the borders by elevation of the epidermis. There was slight inflammatory reaction at the edges. Only in a few lesions was there at any time any evidence of a tendency to heal, and the lesions increased in number and size and became confluent until nearly the whole of the chest and upper part of the back was denuded, as is shown in Figure 2. The appearance of the lesions was so like that of those in one of the cases reported by Brocq that his description may be quoted verbatim for our patient.

"There was a strikingly characteristic appearance of the bullae on the presternal region and about the middle of the back. These bullae, which had appeared several weeks before, had broken, leaving the corpus mucosum and the derma exposed as if a vesicatory had been applied, and far from showing any cicatrization, they were extending at their edges by detaching the epidermis which was raised at the periphery in large shreds. They thus formed large

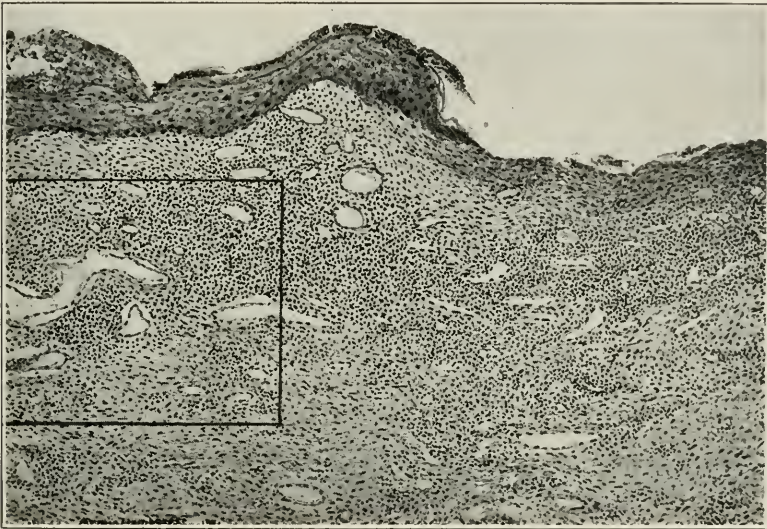


Fig. 3.—(Low power photomicrograph retouched). Margin and base of bleb, showing dilated vessels, diffuse cellular reaction and absence of regenerative activity on the part of the epidermis.

surfaces which, because of the confluence of several lesions, were irregular. The surfaces were raw, oozing, slightly hemorrhagic and very painful."

There were a few small lesions on the upper part of the arm. Except for these there were none on any part of the body except the trunk. The abdomen was not affected. A few days before death a few superficial, and not very painful lesions, appeared on the buccal mucous membrane.

Clinical Course.—During her stay in the hospital the patient continually complained of the painfulness of the lesions on the skin. She was at first not particularly prostrated. There was no marked change in her condition until three or four days before her death when the prostration became much more marked. On Feb. 24, 1921, there was a sudden profuse hemorrhage from the mouth, the source of which was never determined, and on Feb. 25, 1921, she died.

During the two months that she was under our observation various soothing applications were applied with no alleviation of the pain and with no effect on the lesions. Sodium cacodylate was given hypodermically for about two weeks with no effect.

The most striking clinical characteristics were: the extent and painfulness of the lesions, the absence of tendency toward healing, the localization on the trunk, the absence of lesions in the mouth till late in the disease, and the moderate amount of fever.

One of Brocq's patients had only a few lesions in the mouth. Perhaps the absence of teeth in our patient may have partially accounted for the lesions being so few.

No biopsy was made, but permission for a necropsy examination was obtained.

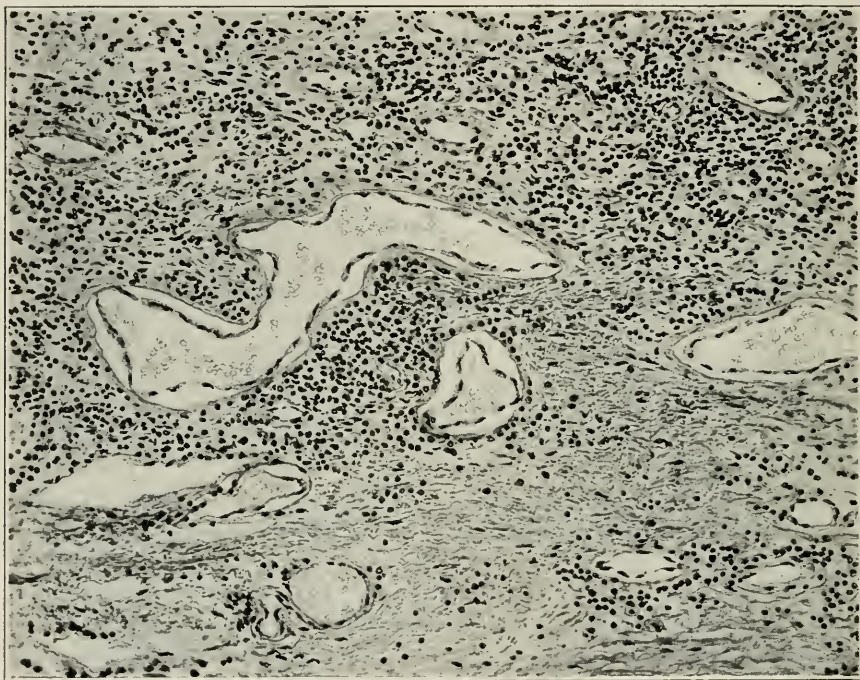


Fig. 4.—Higher magnification of an area in Figure 3. The prominent endothelial lining of the blood vessels and the mononuclear character of the infiltrating cells are well shown.

Necropsy Examination.—The skin lesions, which constituted the most striking gross feature, have already been fully described. It may be added, however, that in removing blocks of skin for histologic study, the superficial character of the lesions could be well demonstrated. The exfoliated tissue seemed to have included only the epidermis. This was clearly so in the case of the denuded patches on the anterior surfaces of the thorax and arms, on which the lesions were quite dry. The exposed derma here was bright red, but strikingly smooth and free from granulations. Over the back there was considerable seropurulent discharge from the raw surfaces and some undermining of the skin edges,

suggesting a more active secondary bacterial infection in the dependent and less protected regions.

The subcutaneous tissues and indeed the tissues in general were unusually dry, and there was little fluid in the stomach and intestines and practically no urine in the bladder (a condition referable no doubt to the painful mouth lesions and the resulting diminished fluid intake).

The gross changes in the thoracic and abdominal viscera were not striking or important, and may be briefly summarized:

There was a general atrophy of the organs of the senile type. The heart weighed only 225 gm. and its musculature was quite dark ("brown atrophy"). The liver and spleen were likewise abnormally small, the former weighing 1000, the latter 38 gm. The kidneys were slightly reduced in size and showed occasional arteriosclerotic scars and several small cysts. There was a moderate



Fig. 5.—(Low power photomicrograph retouched). Intact skin in neighborhood of bleb. The vascular spaces in corium are even more prominent than in the exfoliated areas, but the cellular reaction is less marked. Note the narrow pale fatty zone just beneath the epidermis.

generalized arteriosclerosis. The most marked changes were seen in the respiratory tract. The mucosa of the larynx, trachea and bronchi was reddened and, in the trachea particularly, it had lost its normal lustrous translucency and was quite opaque. There was throughout more or less mucopurulent exudate. Scattered through the lungs were small firm, red patches, the picture of an early hemorrhagic bronchopneumonia.

Microscopically, the only noteworthy findings were in the skin and upper respiratory tract. Skin: A number of sections, including the exfoliative lesions

on the thorax, arms, thigh and adjacent normal looking skin, showed practically the same picture. The most striking feature was the presence of numerous dilated, thin walled blood vessels throughout the corium. These vascular spaces were seen not only in the areas in which the epidermis was lost, that is, the base of the blebs, but extended for considerable distances marginally beneath an intact and apparently only slightly altered epidermis. The size and frequency of these dilated vessels and their relation to the epidermis are well shown in Figures 3 and 5. In places the dilatation was even more marked than these illustrations show.

The endothelial lining of these blood spaces was quite prominent (Fig. 4), so much so that some of the smaller vessels resembled epithelial-lined ducts.

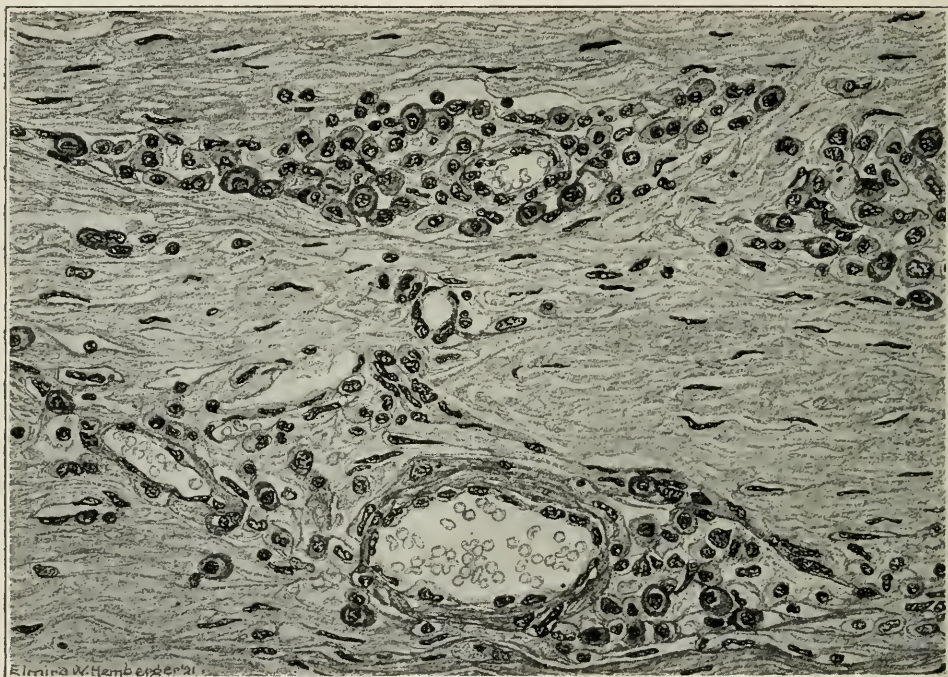


Fig. 6.—(High power drawing). Perivascular infiltration in deeper zone of corium. The cells here as elsewhere are mostly of the plasma cell type.

Fresh fluid blood filled practically all of the spaces. In a few of these just beneath the denuded surface, there was a homogeneous pink staining coagulum, but no definite thrombi were demonstrable.

The second significant feature of the cutaneous lesions was the cellular reaction. There was everywhere more or less round cell infiltration. The cells showed a tendency to a definite perivascular grouping, but in the base of the blebs they were scattered diffusely. The cells varied in type, but the dominant cell was of the plasma cell type (Fig. 6) having a fairly dense round nucleus, somewhat excentrically placed, and a relatively large amount of deeply staining cytoplasm (hematoxylin—eosin preparation). There were a few small lymphocytes and a considerable number of the mononuclear cells of a rather

indifferent type, with vesicular nuclei and irregular pale-staining cytoplasm. No polymorphonuclear leukocytes were seen except in the detritus forming the base of the bleb, and they were scarce even here. Eosinophils, which are rather regularly present in both acute and chronic pemphigus, were rarely seen. There were indeed a few large mononuclear cells which showed a distinct acidophilic and more or less granular cytoplasm, but these were apparently large mononuclear phagocytes which had engulfed red blood cells, and not true eosinophils.

Changes in the connective tissue of the corium were not pronounced. There was relatively slight edema, no evidence of degeneration, and very little proliferative reaction. Fibroblasts were seen here and there, mostly near the denuded surface, but there was not such active proliferation as is commonly associated with ordinary bacterial or chemical injuries of the skin of similar grade, and

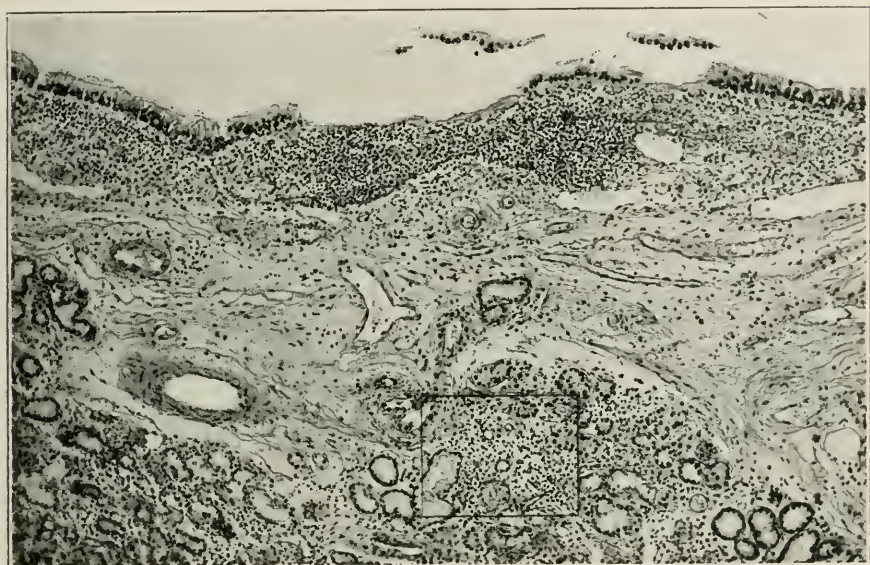


Fig. 7.—(Low power photomicrograph, retouched). Acute and subacute inflammatory reaction in trachea. Mucosa is partially exfoliated with an exudate of polymorphonuclear leukocytes, serum and red blood cells in the superficial zone. Changes in the deeper zone are shown in Figure 8.

there were no budding capillaries. In other words, a true granulation tissue was absent.

The changes in the epidermis were variable. At the margin of the bullae the epidermal layer ended rather abruptly. In some places the free edge was lifted up for a short distance by what was obviously fluid accumulation. There was little evidence of epithelial proliferation. Except near the margins of the blebs, the epithelium showed only moderate degenerative changes, swelling and vacuolization. In general, regressive changes were more marked in the lower layer of the rete mucosum. There was no vesicle formation within the epidermis itself and no cellular infiltration except at the bleb margin.

The papillae were in general flattened and just beneath the basal layer of the rete there was a narrow but well marked fatty reticular zone (Fig. 5). It

seemed possible that this change in the uppermost portion of the corium might represent the first stage of bleb formation, though this is not clear. The epidermis in general was thin, in places only four or five cells thick. This was no doubt a part of the senile atrophy of the tissues and was probably not related to the existing disease.

There was little or no reaction about the sudoriferous glands and the occasional hair follicles, and the nerve bundles were apparently everywhere uninvolved.

Respiratory Tract: Sections of the trachea and bronchi showed evidence of both an acute and a subacute or chronic inflammatory process (Fig. 7). Here and there the epithelial lining was lifted up by serum, and in places there was widespread desquamation. Bacterial stains showed numerous gram-positive

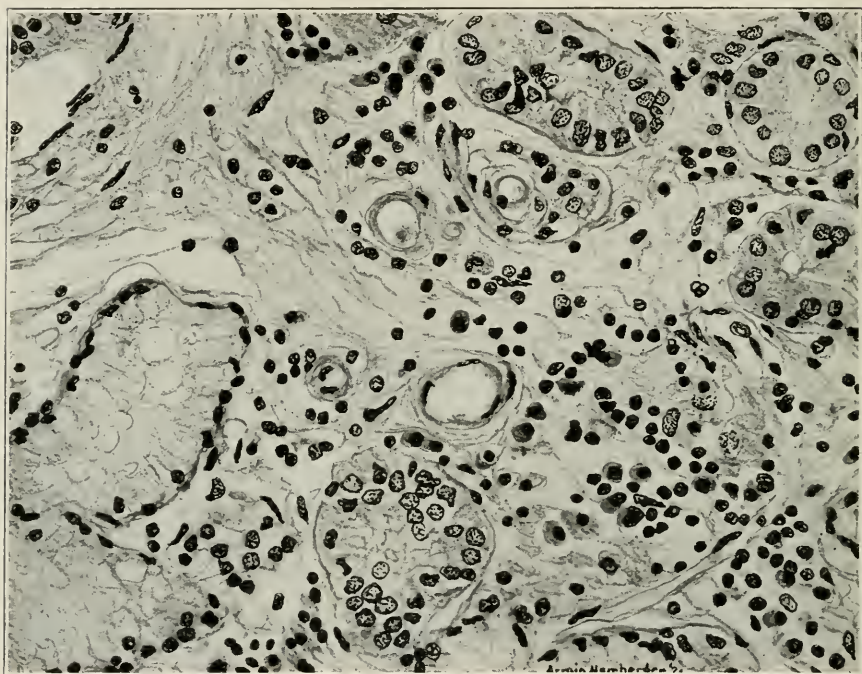


Fig. 8.—Higher magnification of an area in Figure 7 showing edema and mononuclear reaction about the mucous glands. Many of the cells are of the same type as those in the cutaneous lesions.

cocci entangled in the cilia and scattered through the submucosa. Polymorphonuclear leukocytes, fibrin and red blood cells constituted the exudate along the surface and in the superficial layer of the submucosa. In the depths of the submucosa, especially about the mucous glands, there was an infiltration by mononuclear cells, mostly of the plasma cell and lymphocyte types, and edema (Fig. 8). Connective tissue proliferation was slight. This combination of acute and subacute reaction obtained throughout the bronchial tree. In the lungs, there was about the smaller bronchi a patchy exudate into the alveoli, consisting chiefly of red blood cells and polymorphonuclear leukocytes, obviously a terminal process.

DISCUSSION

The histologic picture of the cutaneous lesions in this case correspond in general to that of chronic pemphigus as described by previous investigators.²

It is noteworthy, however, that eosinophils, the presence of which many workers have emphasized, were relatively rare in the sections from our case and that there was no increase of these cells in the blood. Plasma cells, on the contrary, constituted a prominent feature of the cellular reaction.

The widespread lesions in the respiratory tract, pharynx, larynx, trachea and bronchi, we have interpreted as a part of the pemphigus. While there is clearly present an acute bacterial infection—as evidenced by gram-positive cocci in the mucosa—and an acute inflammatory reaction, this is obviously superimposed on a subacute or chronic inflammatory process. The microscopic changes in the submucosa of the trachea and bronchi simulate closely those in the skin and leave little doubt as to their relationship. Pemphigus of the respiratory tract, generally but not always associated with cutaneous lesions, has been described by several investigators,³ but in most cases the changes have not been carefully studied histologically.

While there may have been no previous attempt to separate such cases as Brocq describes into a distinct group, it is probable that most dermatologists of large experience have encountered cases which did not conform to the usual type of chronic pemphigus and which may properly be placed in this group. In this country such cases have usually been grouped under pemphigus vulgaris (chronic or true pemphigus), and have frequently been designated as malignant.

A case of this type, which showed a slight tendency to vegetations in some of the lesions, was reported in 1905 by Ormsby and Bassoe,⁴ who also refer to similar cases. At that time the question was raised as to whether the case should be classed as pemphigus vegetans. Later, in his textbook, Ormsby placed this case under pemphigus vulgaris, remarking:

That certain examples of pemphigus belonging to this group are acute in nature seems to be a fact. A number of cases have been under observation during the past few years. One of these was reported conjointly by the author

2. Spiegler in Mracek: *Handbuch der Hautkrankheiten* 2:23, 1905. Ehrmann und Fick: *Kompndium der Speciellen Histopathologie der Haut*, Wien 1906, p. 13.

3. Trautmann: *Die Krankheiten der Mundhöhle und der oberen Luftwege bei Dermatosen*, Wiesbaden, 1911.

4. Ormsby and Bassoe: A Case of Acute Malignant Pemphigus (P. vegetans?) with Autopsy Report, *J. Cutan. Dis.* 23:294, 1905.

with Dr. Peter Bassoe. In this case the lesions originated in the mouth and the disease proved fatal in two months. Extensive cutaneous involvement occurred with the formation of bullae and severe extensive erosions of the skin. There was practically no attempt at healing in any of the denuded areas. This history could be repeated many times by patients seen during the last few years.⁵

Brocq's articles, by calling attention to this syndrome, may lead to a detailed study of a larger number of cases, which may possibly bring about a more definite conclusion in regard to these cases, though we can expect little information from the study of the histopathology and bacteriology. In one of Brocq's cases there was a growth of a mixture of staphylococci, streptococci, diplococci and bacilli, which he attributes, no doubt correctly, to a contamination from the surface of the body.

Brocq does not pretend to fix this syndrome definitely as a new clinical entity. He simply notes that the appearance and evolution of the syndrome which he sketches seems to be quite characteristic, and inquires whether this syndrome is always a primary condition or whether it may not be sometimes a syndrome which may be grafted on another bullous dermatosis, especially on a dermatitis herpetiformis, dermatite polymorphe or a chronic pemphigus. Among several cases reported, he cites one which tends to support the latter view. And in one patient, an 18 months old child, he questions whether the syndrome was not a variety of impetigo similar to pemphigus neonatorum.

Until some fruitful researches have thrown some light on the etiology and pathogenesis of pemphigus it may be idle to speculate on the place of this group of cases in the general scheme. At present, however, in their clinical characteristics they appear to us to be more closely related to chronic pemphigus and to acute febrile pemphigus.

5. Ormsby, O. S.: *Diseases of the Skin*, Ed. 2, 1921, p. 375.

SYPHILIS AND TUBERCULOSIS

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AND

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The subject, which this communication embraces, is one frequently discussed, but the case reported shows such varied and interesting pathologic manifestations that it seems well worth the effort to compile detailed data on it.

REPORT OF A CASE

History.—R. S., aged 48, colored, a cook and fish peddler, living at Ford City, Pa., was referred to the dermatologic department of the Passavant Hospital of Pittsburgh, Oct. 6, 1920, on account of extensive bilateral ulcerations on his neck.

He gave the following history: About a year ago he noticed a few deep-seated lesions on his face and neck, continuously enlarging. Within four weeks most of these lesions broke down and formed ulcers, which remained in the same condition for a considerable period until the patient's physician gave him seven intravenous injections of arsphenamin; a slight improvement was noted, and the ulcers healed partially except at the nape of the neck and about the ears where they remained unaffected by the treatment and continued to discharge profusely a greenish pus, which was very offensive.

About the time of the appearance of these ulcers, the patient's legs began to swell; this edema was especially noticeable about his ankles; at first it would subside during the night, but during the last three months it became rather stationary, being aggravated only if he was more active than usual. Concurrently with this edema, he noticed, a gradually beginning dyspnea, exaggerated on climbing stairs, with occasional pain in the precordium. All of these symptoms improved after antisyphilitic treatment.

He had been very miserable since the edema became generalized; the greatest inconvenience was caused by the edema about the testicles and penis, interfering with urination. His appetite was good. Bowel movement was interfered with by hemorrhoids, which bled frequently and freely. He tired quickly, slept well and had no headaches.

He had had a chancre ten years ago which had been untreated. Gonorrhea was his "constant companion" as he put it. Outside of these two diseases he had never been ill.

He had been married for twenty-three years; his wife had had four miscarriages, but had no living children. He used tobacco and coffee to excess, and he drank alcoholic beverages in moderation. His father died of cardiac disease. His mother died of tuberculosis. He had five brothers who were well; one brother had died of tuberculosis. One aunt had scrofula.

Physical Examination.—The patient was lying in bed propped on several pillows; his breathing was heavy and labored. Although his entire body was edematous, his face was strangely narrow and thin, and his cheek bones were very prominent. He answered questions very intelligently. He did not look older than his age. The skin all over his body was puffed and there was

marked indentation on pressure; however, it felt very dry and especially over the abdomen it was scaling; the condition had the appearance of ichthyosis simplex. There were three large ulcerative areas on the lateral surface of the neck—one on the right side extending from the clavicle 6 cm. upward and 16 cm. transversely, and two ulcerating surfaces almost sym-

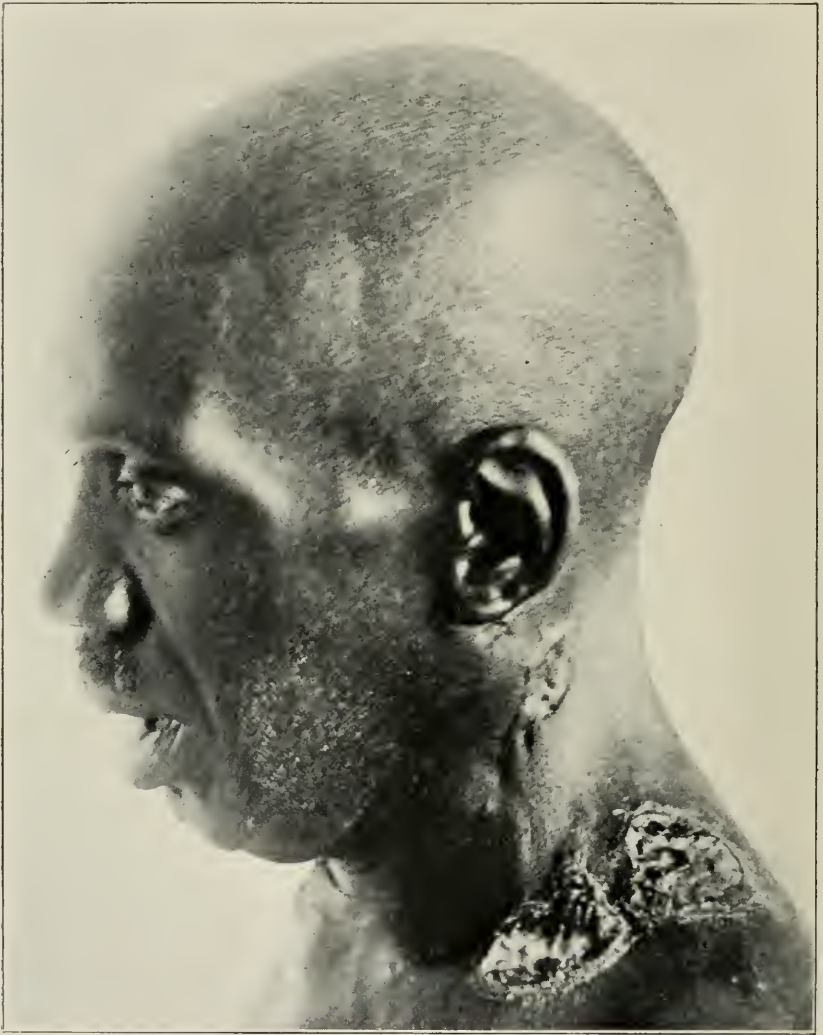


Fig. 1.—Two ulcers on the left side of the neck.

metrically placed to the one on the right side were found on the opposite lateral surface.

The borders of all were irregular, circinate in the large one, kidney shaped in the other two, with deeply punched out uneven edges, definitely undermined; all were partially covered by brownish green crusts, which were easily elevated

and left an uneven reddish-gray base, protruding in areas, depressed elsewhere. There was a profuse discharge, which seemed to pour out of the ulcers, bathing the base.

On either side leading from these areas of ulceration there was a fan-shaped scar which extended to the ear and showed keloid formation in areas. It looked like a healthy scar, the pigmentation of which was much lighter than the surrounding skin.

The eyes reacted to light and accommodation; the elbow and knee reflexes appeared to be normal. The Romberg sign was slightly positive. The gait could not be observed well, as walking caused dyspnea at this time. At a later date his gait was normal.

Laboratory Findings.—The roentgen-ray examination revealed enlarged mediastinal glands, which were probably syphilitic.



Fig. 2—Tuberculosis peritonitis.

Blood examination revealed: red blood cells, 5,100,000; white blood cells, 13,200. The result of the differential count was: polymorphonuclears, 54 per cent.; small mononuclears, 38 per cent., and large mononuclears, 8 per cent. Blood Wassermann reaction: cholestrinized antigen, + + + +; acetone insoluble lipoids, + + + +. The icebox method of fixation yielded the same result.

Urine: Albumin was present. There were a large number of casts.

Diagnosis.—The diagnosis was tertiary syphilis; tuberculonodular ulcerative gummas.

History of Disease and Treatment.—On account of the generalized anasarca, the patient was put on an elimination treatment, sodium citrate, 15 grains, three times a day.

His fluid intake was restricted and one ounce of castor oil was ordered every second day, with absolute rest in bed. In ten days his general condition improved remarkably, and he was put on potassium iodid, 30 grains daily, and increased 3 grains every day.

On the fourteenth day, 0.4 gm. of neo-arsphenamin was given intravenously and again on the eighteenth day. Within twenty-four hours after the second dose of neo-arsphenamin the patient was again water-logged, and albumin was present in his urine. We then decided to discontinue the neo-arsphenamin treatment, and continued administering potassium iodid in increasing doses until the forty-third day. The ulcers had healed and the edema had disappeared; the patient felt well enough to go to his home. He was put on small doses of mercury (*Hydrargyri chloridum corrosivum* 1-16 gm., three times a day and instructed to return to our dispensary once a week. On these visits, after an examination of the urine the patient was given mercury salicylate, 1 grain, intramuscularly. He continued to improve and gain weight and went to work on a wagon the second week in December.



Fig. 3.—Multiple gumma of the liver.

On Jan. 1, 1921, the patient suddenly developed ascites, began to feel dizzy and weak, and was readmitted to the hospital on Jan. 2, 1921.

Three liters of turbid fluid were recovered by paracentesis, after which the patient seemed to improve greatly. Our laboratory reported that the fluid formed a "web" on standing. The smear showed a large number of cells, 95 per cent. of which were small lymphocytes, 4 per cent. endothelial cells and 1 per cent. polymorphonuclears. Wassermann reaction: cholestrinized antigen, + + + +; acetone insoluble lipoids, + + + +. The icebox method yielded the same result. Microscopic examination for tubercle bacillus was negative.

One hundred c.c. of the fluid from the abdomen were centrifuged at high speed for twenty minutes, and the sediment diluted with 2 c.c. of sterile salt

solution. The fluid was injected subcutaneously into the upper left thigh of a guinea-pig after trauma of the lymph nodes in the left groin. Feb. 24, 1921, the pig was alive and well; there was no adenopathy.

A weak and slightly irregular pulse, ranging from 86 to 106, and temperature mostly subnormal, usually about 97 F., but on one occasion rising to 100 F., completed the picture, which the patient presented. He was languid, but showed no sign of acute illness or of oncoming death.

With the report of an exudate, instead of a transudate, which was expected, the diagnosis of hepatic cirrhosis was eliminated, tuberculous peritonitis, which



Fig. 4.—Mediastinal adenopathy before treatment.

was greatly anticipated, was only tentatively made on account of the lack of tenderness in the abdomen.

Within forty-eight hours the patient was so distended again that a second paracentesis was performed, and 2 liters of the same type of fluid was recovered as before.

A further search in order to clear up the diagnosis was made by requesting a comparative roentgen-ray study of the size of the mediastinal glands which on October 7 were definitely hypertrophied. These gland shadows had disappeared

almost entirely or practically so, according to the roentgen-ray findings, and we felt reasonably certain that these glands, which we thought syphilitic, had disappeared under the influence of antisyphilitic treatment.

The further course of this patient was unsatisfactory. He was steadily losing ground until January 12 when the patient became delirious and expired at 1:45 a. m.

Necropsy Findings.—The findings were: tuberculous peritonitis, ulcerative tuberculous enteritis, tuberculous mediastinal and mesenteric adenitis, ulcerative tuberculous pneumonitis (left), ulcerative tuberculous bronchitis, healed tuberculosis of the right lung, chronic fibrous pleuritis (right), chronic interstitial nephritis with parenchymatous degeneration, amyloid infiltration of kidneys, acute localized nephritis (right), amyloid and fatty infiltration of the liver, multiple gummas of the liver with hepar lobatum, gummatous adenitis of the saphenous glands, syphilitic aortitis, slight mitral stenosis.¹

DISCUSSION

There are several points of distinct interest in this case—gumma of the lymph nodes are uncommon enough to merit special mention. We always consider syphilitic scars as healthy ones, in differentiation from tuberculous scars, and usually after a destructive syphilitic process the resultant scar remains healthy. In the present case the ulcerations on the patient's neck occurred within a scar, which gave all the appearance of a healed syphilitic ulcer and with which the history of the patient was consistent. At the beginning of the skin manifestations, that is one year before the patient's death, these ulcerations began and under antisyphilitic treatment became absorbed. This happened during the first sojourn of the patient in the hospital, when these ulcerations healed well and quickly under mild antisppecific treatment. The bilateral character of a tertiary syphilitic manifestation of the same character is also not frequent enough so that a notation should not be necessary.

We believe that the mediastinal adenitis revealed by the roentgen-ray examination, which was attributed at that time to a syphilitic process and its later disappearance to antisyphilitic treatment, should be considered in a different light. At necropsy these glands were found to be caseating and gave a typical picture of tuberculosis. At the time of the first roentgen-ray examination they were probably edematous, entering into the general picture of anasarca; later their size lessened, when this vascular syndrome was brought under control.

The question of medication is worthy of discussion. Here we had a patient in need of active treatment, whose kidney function was so interfered with that both mercury and arsenic could be administered only cautiously or not at all. Two doses of neo-arsphenamin produced a generalized anasarca so that we had to discontinue this type of therapy.

1. We find it necessary to confine ourselves to the mere enumeration of pathologic findings on account of brevity. A detailed report of the necropsy findings will be furnished on request.

Urine showing the presence of continued albumin kept us at bay with mercury at the institution of his treatment. Iodids were the only therapeutic measure left. Clinical experience teaches the inadvisability of administration of iodids in tuberculous patients, and the only reason we can give for their administration was that at the institution in which this patient was treated we could see no contraindication. His fairly normal temperature and lack of other symptoms or physical signs put us off our guard. The very fact that the patient continued to improve under the effect of iodids, by the recession of anasarca, dyspnea, healing of ulcers, and the feeling of well being, the gain in strength (physical) and weight did not show that the iodids might defeat our purpose.

His sudden collapse, after about four weeks of well being, and the marked nature of his miliary tuberculosis, on the other hand, seem to indicate that the body which was able to withstand the assaults of this double infection in a fairly efficient manner for years lost resisting ability all at once as it seemed and permitted an unchecked spread of tuberculosis in an uncontrollable manner. How much of this was caused or facilitated by the administration of iodids, as much as 90 grains a day being given, can only be assumed.

Literature is swarming with observations and statistics of the frequency with which these two diseases exist concurrently in the same person.

Ravogli² says in many cases tuberculosis is also associated with syphilis, and together they cause the most hideous ulcers and extensive destructions, especially at the vulva.

He³ also states that tuberculosis has a great influence on the course and malignancy of syphilis. It seems that the tubercle bacillus, in consequence of the new syphilitic infection, takes on an extraordinary activity, and in this way syphilis assumes malignant forms. Tuberculosis which was latent during good health, in consequence of the syphilitic infection shows itself with quick and destructive results. It is incredible that the two infections have such a direct influence on one another that when syphilis runs a severe course tuberculosis usually supervenes and ends the life of the patient.

Ravogli⁴ also quotes Hochsinger, who found in children with hereditary syphilis a favorable ground for the reception and development of tuberculosis.

2. Ravogli, A.: *Syphilis in Its Medical, Medicolegal and Sociological Aspects*, New York, The Grafton Press, 1907, p. 58.

3. Ravogli, A.: *Syphilis in Its Medical, Medicolegal and Sociological Aspects*, p. 140.

4. Ravogli, A.: *Syphilis in Its Medical, Medicolegal and Sociological Aspects*, p. 165.

Morris⁵ asserts that syphilis predisposes to tuberculosis.

Vedder⁶ says that "Syphilis makes the bed for tuberculosis." He quotes Brock who, after investigating 7,660 consecutive South African natives among whom tuberculosis was practically unknown at that time, comes to the following conclusions:

1. Thirty-five per cent. of natives have a fibroid condition of the lungs.

2. Sixty-eight per cent. have indurated enlargement of the epitrochlear gland.

3. Both conditions result from syphilis, and nearly 80 per cent. of the natives have one or both conditions.

4. Syphilis prepares the way for tuberculosis and is in all probability the chief cause for the great prevalence of, and the high mortality from, the latter disease in the natives engaged in mine work on the Rand.

5. Syphilis plays a rôle in the production of lung diseases in the youth and adult, the great importance of which has not been recognized.

In accordance with such considerations, it would be expected that syphilis would be more prevalent among the tuberculous than among those suffering from other diseases.

Letulle, Bergeson and Lepine,⁶ who for more than a year performed Wassermann tests on all patients with tuberculosis, obtained positive reactions in 19 per cent.

Marino and Fournier⁷ emphasize the unsuspected frequency of inherited syphilis as a predisposing factor in status lymphaticus, asthenia and obscure endocrine derangements. Tuberculosis so often develops on a basis of syphilis that inherited syphilis should be suspected in masked cases.

In analyzing these reports of cases of tuberculous patients in whom the blood Wassermann test was performed, we have placed them in two columns: (1) those who gave unmistakable evidence of syphilis by a strong blood Wassermann reaction; these were placed in the column of "Positively Syphilitic"; (2) those who gave a lesser blood Wassermann reaction; these were placed in the "Probably Syphilitic" column.

5. Morris, Sir Malcolm: *The Nation's Health*, New York, Funk and Wagnalls Co., p. 28.

6. Vedder, Edward B.: *Syphilis and Public Health*, Philadelphia, Lea and Febiger, 1918, p. 68.

7. Marino, E., and Mussio-Fournier, M. J. C.: *Syphilis and Tuberculosis*, Bull. et mém. Soc. méd. d. hôp. **43**:1002 (Nov. 28) 1919; abstr., J. A. M. A. **74**:359 (Jan. 31) 1920; also in Rev. méd. del Uruguay **22**:807, (Nov.) 1919; also in *Semana méd.* **27**:170 (Jan. 29) 1920; abstr., J. A. M. A. **75**:138 (July 10) 1920.

Percentage is also figured accordingly. Of the 6,324 cases examined, 494 were found definitely syphilitic, excluding 251 cases of Jones and 376 cases of Petroff. On account of lack of differentiation of strength of the blood Wassermann reaction, we find that the average of all investigators studied is 10.36 per cent. Combining the probable and positive cases, we find that of the 6,324 cases, 830 gave a positive blood Wassermann reaction of any strength; this would raise our figures to 17.81 per cent. in the total of all the cases investigated by the authors mentioned in the foregoing.

The frequency of this coexistence of diseases is well known to pathologists, who usually find many pathologic conditions in patients after death, who were not suspected of such multiplicity of lesions. This is by no means unobserved by clinicians, but we feel that it is not emphasized frequently enough.

The following table was compiled to obtain a fair average of the reports of coincidence of these two diseases.

COINCIDENCE OF TUBERCULOSIS AND SYPHILIS

Investigator	Number of Patients	Number Positively Syphilitic	Number Probably Syphilitic	Both	Positive Percentage	Total Percentage
Lettule, Bergeron and Le-pine *	346	64	...	64	19.0	19.0
Vedder *	211	36	17	53	17.0	23.2
Snow and Cooper *	290	44	14	58	14.8	20.0
Lyons *	471	29	12	41	6.2	9.2
Jones *						
Dispensary.....	251	...	73	73	29.0
Hospital.....	189	18	...	18	11.0	25.0
Petroff *	376	...	82	82	21.8
Ford *	328	6	22	28	2.0	8.0
Collectanea, * N. Y. Med. J. ..	175	14	9	23	8.0	13.1
H. J. Cooper *	2,794	181	...	181	6.5	6.5
Day, A. B. and McNutt, W. †	893	102	107	209	11.3	23.4
	6,324	494	...	830	10.36	17.81

* Vedder, Edward B.: Syphilis and Public Health, Philadelphia, Lea and Febiger, 1918, pp. 68, 69, 70 and 107.

† Day, A. B., and McNutt, W.: The Incidence of Syphilis as Manifested by Routine Wassermann Reaction in Two Thousand Nine Hundred and Twenty-Five Hospital and Dispensary Medical Cases, Trans. Assn. Am. Physicians, 34: 345-352, 1919.

CONCLUSIONS

1. A case has been presented in which the patient showed gross syphilitic and tuberculous lesions.

2. Available statistics of the coexistence of syphilis and tuberculosis have been reviewed.

3. The possible malignancy of tuberculosis in the case described is attributed in part at least to iodid medication.

We wish to express our thanks to George W. Grier, M.D., for the roentgen-ray study of this case.

SYNOVIAL LESIONS OF THE SKIN

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AND

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Attention was first called to synovial lesions of the skin by Hyde¹ in 1883. More recently the subject has been discussed by Lingenfelter,² Ormsby,³ and Sutton.⁴

Synovial lesions of the skin occur over the dorsal aspects of the interphalangeal, metacarpo-phalangeal and metatarso-phalangeal articulations. The most frequent situation is over the dorsum of the articulation between the distal and adjacent phalanges of the index finger and thumb.

There is usually a history, extending at least over several months, of the appearance in one of these situations of a small, globular projection from the skin, which is insensitive unless roughly handled, and which slowly develops to the size of a large pea. When punctured a syrupy, whitish, yellowish or brownish, fluid exudes, occasionally mingled with masses like sago grains. As the lesion develops, it ordinarily assumes the appearance of a vesicle or bulla; some lesions have only an epidermic roof-wall and are exceedingly painful, especially when on the feet. The surface of the lesion is generally smooth and shiny and shows more or less telangiectasia. It may appear roughened or moderately verrucous. It may therefore be slightly warty in appearance, but it is more likely to suggest a thick-walled cyst. The lesion is usually translucent or semitranslucent. Fluctuation is usually present, but there are no signs of infection. Bacteriologic examinations of the fluid have yielded negative results in the cases cited by Drs. Ormsby and Lingenfelter. Immediately subsequent to puncture the cyst collapses, but after the lapse of a week or more the cavity refills with a similar gelatinous, glairy fluid.

The pathogenesis is problematical. Anatomically there are no well-defined bursae in these situations; the lesions that have been radiographed show apparent relationship to the underlying articulations.

Ganglions of the fingers most frequently occur on the flexor aspects, and often show similar connections with the adjacent joint cavities.

1. Hyde: *Diseases of the Skin*, Ed. 1, Philadelphia, 1883, p. 444.

2. Lingenfelter: *Jour. Cutan. Dis.* **31**:647, 1913.

3. Ormsby: *Jour. Cutan. Dis.* **31**:943, 1913.

4. Sutton: *Diseases of the Skin*, Ed. 3, St. Louis, The C. V. Mosby Co., 1919, p. 436.



Fig. 1 (Case 1).—Lesion on middle finger of the right hand.



Fig. 2 (Case 1).—Roentgenogram of lesion.

They have been regarded by many as herniae of the synovial membrane of a joint or tendon sheath through its capsule or fibrous sheath, described by Jordan as "a sudden extrusion of the synovial membrane through a chink in the capsule of a joint or tendon sheath." Later a plastic inflammation closes the outlet. Other observers believe that certain folds and crypts, occurring in synovial membrane lining joints and tendon sheaths, are of such a character that pockets of unobliterated synovial membrane may be occluded by inflammatory adhesions in the outlets of the crypts or folds leading to the synovial cavity. As the synovial membrane continues to secrete, a cyst is formed away from the joint or tendon sheath.

Adventitious bursae frequently occur in areas in which anatomic or regularly described bursae are never found, particularly over bony prominences subjected to pressure or friction for long periods of time. Clarke⁵ states that "the development of an adventitious bursa takes place through a physiological metamorphosis in the connective tissue cells to meet the requirements of the body, similar to the development of an anatomical bursa," and he does not believe that they are formed by cystic degeneration of connective tissue as ganglions frequently are. Fetal sequestration has also been mentioned as a cause of ganglions, as in dermoid cysts. Clarke is "positive that many ganglia are distended anatomical or adventitious bursae, but the majority are connective tissue cysts, formed by degeneration excited by unknown factors. Ganglia are very rarely hernial protrusions."

Most synovial lesions of the skin originate from, or are distended, hydropic adventitious or anatomic, bursae. Some of them seem to show, roentgenographically, connections with the joints. If these connections have been patulous, they have been closed because pressure on the cysts does not show any patent connection with the articular cavity. In their articular relations the synovial lesions of the skin suggest a relationship to ganglions.

AUTHORS' CASES

The condition is rare, or at least uncommon. We have seen two cases. The first was of twenty years' duration. The lesion occurred in a man 26 years of age, and was situated over the dorsal aspect of the distal interphalangeal articulation of the middle finger of the right hand. It consisted of a pea-sized, smooth, shiny, transluscent, rounded, cystic tumor with a thick wall; it was not painful; there were a few visible venules in its wall. On palpation the tumor was firm but not hard. There was a sense of fluctuation.

5. Clarke: *The Pathogenesis of Ganglia*, Surg., Gynec. & Obst., July, 1908, p. 56.



Fig. 3 (Case 2).—Patient's right hand before and after treatment.



Fig. 4.—*a*, roentgenogram of portion of right index finger before treatment, *b* and *c*, side and front view after treatment.



Fig. 5.—Lesion on right middle finger (Dr. Pusey's case).

The second case was of five months' duration, and occurred in a woman 48 years of age. The lesion was situated over the dorsal surface of the distal interphalangeal joint of the right index finger. It was painless, globular, tense, semitranslucent, pearly in color, and the size of a large pea. Pressure caused a hyperemic areola at its circumference and a pallor of its central portion. This was probably caused by the occlusion of the small vessels in the walls of the lesion. The walls were thick, tough, smooth, shiny and slightly telangiectatic. Fluctuation was present.

Roentgenograms of each of these cases, as in the case described by Lingenfelter, showed no bone involvement; but the roentgenograms in both our cases showed plainly a connection with the joint cavity.



Fig. 6.—Lesion on right middle finger (Dr. Pusey's case).

DR. PUSEY'S CASES

Through the kindness of Dr. William Allen Pusey, we include herewith a description of two cases of synovial lesions of the skin occurring in man and wife. This peculiar coincidence is itself worth recording. Clinically the lesions resembled our two cases. We are fortunate in being able to present photographs of each case (Fig. 5, husband, and Fig. 6, wife). The histopathology of Figure 6 as recorded by Dr. Pusey follows:

The sections show a sharply circumscribed fibrous tissue growth, the central part of which appears to have undergone myxomatous degeneration. In this myxomatous tissue there are several cysts, the walls of which are formed by compression of the surrounding myxomatous tissue. These cysts have no

endothelial or epithelial lining, nor do they or the tumor itself show any connection with a deeper structure. The whole tumor has compressed the surrounding tissue more or less; especially is this well marked in the lower part of the section where coil glands are found in this compressed wall.

TREATMENT

The treatment requires the complete destruction or excision of the entire secreting cyst wall. Lesions have been carefully dissected out, but the removal must be complete or recurrence takes place. Our first patient was so treated, and there was no recurrence. Roentgenotherapy is the method of choice. Hyde and Ormsby employed unfiltered roentgen rays successfully in several cases; the technic was fractional (several small doses). Sutton used radium with satisfactory results in one case (40 milligram hours, unscreened).

The lesions in our second case disappeared completely after one roentgen-ray exposure. The technic was: A dose of 1 Holzknacht unit skin distance (one skin unit) unfiltered was applied to each side of the tumor. The articulation was included in the field of radiation. Four weeks after this "cross-fire" treatment the lesion had completely disappeared, and a second exposure of 1 Holzknacht unit skin distance, unfiltered, was given to its previous site. A roentgenogram two weeks later showed that the subcutaneous portion, which was connected with the joint, had entirely disappeared.

Refrigeration (carbon-dioxid snow) and electrolysis have been used.⁶

6. In addition to the references given, the following may be of interest:

Jones and Meakins: Cited by Hyde.

Jordan: Ganglion, *Lancet* 2:242, 1893.

STOMATITIS AND APLASTIC ANEMIA DUE TO NEO-ARSPHENAMIN *

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Among the late reactions occurring after the use of arsphenamin products in the treatment of syphilis, the most serious are dermatitis, stomatitis, jaundice and encephalitis. In this country the last is rarely encountered, although it is apparently quite frequent in Europe. The other reactions mentioned are more common and are thus of greater practical importance. Dermatitis and stomatitis appear to be closely allied. Previous papers¹ from this clinic have discussed this interrelation, and have drawn attention to a characteristic common to both types of reaction, namely, a striking alteration in the blood picture during life and marked changes in the bone marrow at necropsy.

Since any data which may tend to throw light on the mechanism of these reactions should be presented, the following case report is believed to be worthy of record.

REPORT OF A CASE

History.—A white woman, aged 50, had been twice married. The first husband had died some years ago, cause unknown. The issue from this marriage was one daughter, well at the age of 28, with no stigmas of congenital syphilis, who herself has several normal children. During the first marriage there were no miscarriages and no history of possible signs of syphilis.

In 1918, the patient married again, a marriage of convenience, with a man twelve years her senior. Owing to the character of the marriage there was no sexual intercourse until February, 1919, and this took place only once. Intromission was not effected, but ejaculation took place, and semen was deposited on the vulva. At the time the patient had an open abrasion on the inner surface of one labium majus. A few weeks later, after the abrasion had healed, there appeared in its exact location a small painless erosion. This was followed in a few weeks by general malaise and headache. In May, 1919, she was seen by one of us.

Physical Status.—The patient was obese, but was otherwise in excellent physical condition. Examination of the central nervous system and of the cardiovascular system were negative. On the inner surface of the left labium majus near the fourchet was a small oval erosion about 0.75 by 1.0 cm.,

* From the Syphilis Department of the Medical Clinic, Johns Hopkins Hospital.

1. Moore, J. E., and Foley, F. E. B.: Serious Reactions from the Salvarsan and Diarsenol Brands of Arsphenamin: Unusual Blood Pictures with the Report of a Fatal Case, *Arch. Dermat. & Syph.* **1**:25 (Jan.) 1920. Moore, J. E., and Keidel, A.: Dermatitis and Allied Reactions Following the Arsenical Treatment of Syphilis, to appear in *Arch. Int. Med.*

slightly elevated, dusky red, indurated and painless. There was slight painless discrete left inguinal adenopathy. Careful examination of the skin, mucous membranes and glands failed to disclose any secondary manifestations. Dark-field examination of the secretion from the labial lesion showed many actively motile *Spirochaeta pallidae*. The blood Wassermann reaction was positive.

The husband denied any definite history of syphilis but admitted several genital sores early in life. Examination revealed anisocoria, sluggish irregular pupils, and sluggish knee and ankle jerks, more active on the left. The gonads were normal to palpation. The blood Wassermann reaction was positive, but spinal puncture was refused. However, evidence corroborating the clinical diagnosis of neurosyphilis was obtained by the fact that this patient was Wassermann-fast. Twenty-four doses of arsphenamin with interim mercury by inunction failed to reverse the positive blood Wassermann reaction.

TABLE 1.—TREATMENT ADMINISTERED

Date, 1919	Drug	Blood Wassermann Reaction	Remarks
May 17	Arsphenamin 0.4 gm.	Positive	Slight erythematous rash, appearing 24 hours after treatment, lasting 36 hours
May 21	Arsphenamin 0.3 gm.	Positive	Recurrence of skin rash, maculopapular rash of greater intensity, lasting 4 days, and accompanied by much itching
May-Nov. inclusive	Mercurial oint- ment 33%		
July 2	Negative	
Sept. 3	Negative	
Dec. 6	Neo-arsphenamin 0.3 gm.	Negative	No generalized skin rash. Two days later profuse crop of herpes, upper lip; also coryza, which may have caused herpes. About 5 hours after the injection, chill, nausea and headache, and for the next 3 to 4 days generally knocked out
1920			
Jan. 6	Neo-arsphenamin 0.3 gm.	Anticomple- mentary	After this and each succeeding treatment, marked malaise lasting several days
Jan. 16	Neo-arsphenamin 0.3 gm.		
Jan. 26	Neo-arsphenamin 0.15 gm.	Anticomple- mentary	
Jan. 30- Feb. 10	Influenza
Feb. 26	Negative	
Feb. 25- April 15	Mercurial oint- ment 33%		
April 15	Neo-arsphenamin 0.3 gm.	Negative	
April 28	Neo-arsphenamin 0.3 gm.	Negative	
May 10	Neo-arsphenamin 0.3 gm.	Negative	
May 15	Neo-arsphenamin 0.3 gm.	Negative	
May 25	Neo-arsphenamin 0.3 gm.	Negative	See text

Diagnosis: Primary syphilis, contracted by seminal injection.

Treatment and Course.—Treatment was begun on the day of the first visit and was continued as shown in Table 1.

After the last treatment, on May 25, the patient left Baltimore for the seashore, where she remained a week. On the train, about six hours after the treatment, she suffered with chilly sensations and vertigo. Within a day or so after her arrival at the shore, she felt miserable and for the next week had some fever, her mouth became sore, and she gradually became jaundiced. On June 2, she returned to Baltimore, and was seen late that evening at her hotel.

Her temperature was 101 F., pulse 110. The skin and sclerae were slightly jaundiced. The gums were tender, swollen and bleeding, and the teeth were loose. Around the first upper left molar was a purplish discoloration, and on the hard palate was a huge ecchymosis. Small purpuric spots covered the hands and arms, and there was a large ecchymosis of the left shoulder. During the next two weeks she grew steadily worse and gradually became profoundly ill. Her temperature remained constantly elevated, ranging from 101 to 105 F. Fresh hemorrhages, petechial and ecchymotic, constantly appeared in the skin and mucous membranes, and there was intermittently severe epistaxis, bleeding from the gums and vagina. Blood was found in the urine and stools. The condition of the mouth grew much worse. The gums became purplish red, covered with a thick purulent discharge; the teeth were loose; a large

TABLE 2.—STUDIES OF THE BLOOD

Date	Red Blood Cells	Hemoglobin, per Cent.	White Blood Cells	Differential, per Cent.						Platelets	Remarks	Mention
				P. M. N.	P. M. B.	P. M. E.	S. M.	L. M. T.	Myob.			
May 25		Neo-arsphen- amin 0.3 gm.
June 4	3,176,000	61	1,100	11.0	—	5.0	76.0	8.0	—	None seen		
June 5	3,832,000	75	1,600	17.0	—	4.0	79.0	3.0	—	None seen		
June 6	Transfusion 1	
June 7	4,128,000	81	1,000	15.0	—	—	78.0	7.0	—	None seen		
June 9	4,102,000	79	800	Coagulation time (Hoggs) 6 min.	Transfusion 2
June 10	3,856,000	76	600	10.6	—	1.3	81.4	5.4	1.3	48,000		
June 12	4,112,000	74	800	9.0	—	—	89.0	2.0	—		
June 14	3,456,000	78	950	12.0	—	2.0	83.0	3.0	—		
June 16	3,616,000	83	950	5.0	—	2.0	91.0	2.0	—	Coagulation time 7 minutes Vital staining reticulated cells 0.4 per cent.	Transfusion 3
June 17	4,000,000	48,000	Reticulated cells 0	
June 18	3,872,000	81	550	4.0	..	—	94.0	2.0	—	28,000		
June 19	3,920,000	36,800	Reticulated cells 0	Transfusion 4
June 20	2,902,000	76	900	6.0	—	—	92.0	2.0	—	28,800		
June 21	3,000,000		
June 22	Died	

necrotic ulcer appeared in the hard palate. Two small pinhead-sized ulcers appeared on the skin, at the angle of the mouth and on one ala nasi, and rapidly increased in size until each was as large as a dime. The base of each was black, composed of necrotic tissue resembling an eschar. Drowsiness was a constant and marked feature, and toward the end the patient complained bitterly of headache. Examination of the heart, lungs and abdomen was always negative.

Treatment was symptomatic only. On June 6, 9, 16 and 19 transfusions of 250 c.c. each of matched citrated blood (Group 4) were administered, without reaction or beneficial effect. The patient gradually grew weaker and died on June 22, four weeks after the onset of the reaction.

Laboratory Data.—Smear from the exudate about the teeth showed many spirochetes and fusiform bacilli, a typical picture of Vincent's angina.

Urine: Specific gravity was low and fixed (1.002 to 1.010). There was a constant trace of albumin, and after June 10 numerous red blood cells and a strongly positive benzidin test. Phthalein (June 9) was 55 per cent. in two hours.

Stool: June 11, there were no blood (benzidin), ova or parasites. June 18, there was bloody mucus, benzidin positive. Thereafter blood was constant.

Blood Culture: June 8, the culture was negative. June 19, Friedländer's bacillus (agonal invader?) was found.

Blood Chemistry: June 12, calcium, 9.7 mg. per 100 c.c. (normal limits), was found.

Blood: See Table 2.

Necropsy Examination (Dr. Webster).—This was performed ninety minutes after death.

Anatomic Diagnosis: The diagnosis was: extensive subcutaneous and subserous hemorrhages; submucous hemorrhages of stomach, intestines and liver; hemorrhagic nephritis; aplastic bone marrow; lobular pneumonia; edema of lungs; arteriosclerosis.

Body: Numerous large and small petechiae were seen in the skin over the posterior surface of the arms and over the chest and abdomen. The skin of the face and neck was lemon yellow, and over the chest and abdomen, subicteric. The subcutaneous tissues were not edematous. The sclerae and conjunctivae were distinctly yellow. The external nares were occluded by recent hemorrhagic clots and were surrounded by scaly excoriations. There was an ulcer about 1 cm. in diameter on the left side of the nose. Its skin edges were purplish, its base formed by granulation tissue. The entire left side of the nose appeared purplish. A similar ulcer appeared on the mucocutaneous border of the mouth at the right side. The mucous membranes of the mouth were roughened and ulcerated and covered with a purulent material which was also oozing from the region of the gums. On the sides of the neck were a number of small indurated purplish areas.

On opening the peritoneal cavity the serous surfaces appeared smooth and transparent. No free fluid was seen. The small intestines appeared dark, and the transverse colon showed a number of hemorrhages beneath the serosa. The liver and spleen did not extend below the costal margin. On opening the chest cavities no free fluid was seen. The pleural surfaces were delicate and transparent and showed extensive hemorrhages both in the visceral and the parietal layers.

Heart: The heart weighed 325 gm. Its epicardial surface was smooth and glistening, showing large and small ecchymoses toward the base. On section the endocardium was also transparent and normal in appearance, although it covered a number of large and small hemorrhages. The cardiac chambers were not dilated or hypertrophied. The valve leaflets were normal. At the base of the aortic and mitral valves a number of atheromatous patches were seen. The coronary arteries also showed signs of arteriosclerosis. The base of the aorta, however, was elastic and lined with a smooth intima.

Aorta: The aorta had lost its elasticity. On section it presented a remarkable picture of advanced and extensive arteriosclerosis. Waxy patches were seen about the orifices of the smaller vessels. Atheromatous ulcers, fresh and hemorrhagic, were seen throughout its length. One in particular, near the bifurcation, had ruptured through the intima and media, leaving only the thin adventitia.

Lungs: The lungs were deeply pigmented and heavy. Beneath the pleura, particularly of the lower lobes, petechiae and ecchymoses were numerous. On

palpation several irregular nodules were felt in the lower lobes. On section the lower lobes were found to be congested and showed a few irregularly outlined areas of consolidation about the smaller bronchi. Both lungs were soggy and exuded a large amount of fluid, and the alveoli contained a gelatinous semifluid substance. The bronchi were slightly injected.

Spleen: Its capsule was wrinkled and slightly roughened. On section the cut surface was found to be deep red and firm. The trabeculae and blood vessels and malpighian bodies stood out sharply.

Liver: The liver weighed 1,800 gm. and measured 20 by 22 by 10 cm. Its capsule was delicate and transparent. On section the cut surface appeared pale and firm and showed the usual architecture. The lobules stood out distinctly. There was no increase in connective tissue and no areas of necrosis were present. Scattered about were a number of indefinitely outlined hemorrhages.

Suprarenals: The suprarenals weighed 15 gm. each and were normal externally and on section.

Kidneys: The kidneys weighed 120 gm. each and measured 11 by 6 by 3 cm. The capsule stripped easily, showing a number of small petechiae scattered over the surface. On section the cortex measured about 1.5 cm. in thickness. The striae were parallel and regular. The glomeruli were distinct. Here, also, small hemorrhages were observed. Deep in the pyramids were several large extravasations of fresh blood. The blood in the larger veins had clotted and distended the lumina. The pelvis, however, were smoothly lined and appeared normal. The ureters also showed nothing unusual.

Gastro-Intestinal Tract: The esophagus was normal. The mucous membrane of the stomach showed most extensive hemorrhages, large and small, just beneath the surface. The lumen contained a large amount of hemorrhagic fluid. The remainder of the small intestine was filled with dark clotted fluid which stopped rather abruptly at the ileocecal valve. In the region of the transverse colon and rectum other submucous hemorrhages were seen.

Lymph Glands: The lymph glands were examined carefully and did not appear enlarged. The superficial and deep nodes, however, were red and unusually firm.

Brain: The meninges were normal. There was no thrombosis in the sinuses. Over the convexity just beneath the dura was a small collection of fresh blood which might or might not have been there before death. The convolutions were not flattened. No areas of softening were seen. The blood vessels at the base showed extensive arteriosclerotic changes.

Bone Marrow: The bone marrow from the ribs was red. The cavity of the femur, however, contained only a large amount of fat in which an occasional reddish collection of active marrow was seen.

Microscopic Notes (We are indebted for the following careful description to Dr. W. G. McCallum, who kindly reviewed the available material):

Bone Marrow: The sections were made from the bone marrow of the femur which was practically entirely composed of fat. There were, in crevices between the fat globules and around the small vessels, sparse accumulations of cells which at first sight seemed to be all of one type. In sections stained successfully with Wright's stain among these cells no megalocaryocytes were found, no nucleated red cells, no eosinophil myelocytes and only rarely a neutrophil myelocyte of normal appearance. Most of the cells were rather smaller than myelocytes and had relatively large rounded, eccentric nuclei which were sharply outlined and filled with large scattered blocks of chromatin, such as are seen in plasma cells. In this respect they differed from normal myelocytes seen in control sections of bone marrow, since in those cells the nucleus was

more delicately stained, with a clearly defined nucleolus and finely divided chromatin particles. The cytoplasm took a purplish stain, usually without definite evidence of the presence of granules. There was sometimes a pale area about the nucleus. It seemed possible that these cells might be regarded as the basophilic ancestral cells of myelocytes, although they did not correspond with the ordinary descriptions of myeloblasts. A few true myelocytes were discoverable after much search.

It appeared that the bone marrow of the femur at least had ceased entirely to produce the elements of the blood, and any blood formation must be looked for in the bone marrow of the vertebrae and short bones, which was described as red.

Blood formation might also be looked for in the spleen and liver.

Spleen: The spleen was uniform in appearance throughout various sections. The trabeculae, and especially the blood vessel walls, showed rather extensive hyalin changes which became very conspicuous in some sections stained faintly by Wright's stain. The malpighian bodies were rather small but otherwise unchanged. The splenic pulp was fairly full of blood in the sinuses, and there were some extravasations of red corpuscles into the substance. There were numerous minute collections of bacilli in the pulp, surrounded by necrotic cells but by no inflammatory reaction. Between the venules the splenic reticulum contained numerous deeply stained cells exactly resembling those found in the bone marrow. These rather large cells formed conspicuous strands and masses between the venules and were occasionally found within them. Their cytoplasm was basophilic but not distinctly granular, and their nuclei contained abundant large blocks of deeply stained chromatin. They, too, occasionally showed an eccentric pale halo about the nucleus. In most respects they were like plasma cells but they were less regular in form and size and were not obviously and definitely plasma cells.

Liver: The liver showed several large areas of necrosis in each section. These were formed about great masses of bacteria which were chiefly staphylococci, but which were mixed about the edges with abundant bacilli. It will be remembered that in the spleen and kidney only bacilli were found. There was no reaction about the necrotic areas. The tissue in general looked normal so that the bile ducts and portal veins appeared to run in wide bands of connective tissue. This was infiltrated in places with cells which entirely resembled those seen in the splenic pulp. None of these cells were found in the capillaries of the liver lobules.

Kidney: In general the kidney was normal. The epithelium of the tubules was spread apart by dilatation of the convoluted tubules, but it was not markedly degenerated. There were a few scarred areas in which wandering cells were abundant. They had the character of those described in the portal spaces. There were a few small clumps of bacilli with minimal surrounding areas of destruction of the cells.

Lungs: The lungs were extremely edematous, the alveoli being filled with a bloody fluid. Most of the red corpuscles were still visible, but extensive laking seemed to have occurred. There were masses of bacilli scattered everywhere in the alveoli, but there was no pneumonic reaction.

Lymph Glands: The lymph glands were little altered; the lymph cords contained only lymphocytes, and the sinuses were practically empty. There were no large cells like those described. In the mesenteric glands, however, the sinuses contained numerous large phagocytic cells.

DISCUSSION

This case provides confirmatory evidence of points developed in our previous communications.¹ The blood picture is the same as that observed in other cases of stomatitis and of dermatitis exfoliativa. Platelet counts, which were unfortunately lacking in our earlier cases, are provided; they explain the tendency to hemorrhage often noted in cases of this general group. The condition of the bone marrow at necropsy confirms the observation previously made that death may be due to aplastic anemia alone; or, as shown by the absence of inflammatory reaction about the foci of bacteria in the lungs, liver, and spleen, it may result from the destruction of the bodily defense mechanism against bacterial invasion, in which the bone marrow is chiefly concerned.

A careful search of the literature has revealed only three reports of similar cases, aside from those already reported from this clinic.

Labbé and Langlois² report the case of a young woman with secondary syphilis, whose treatment consisted of sixteen injections of neo-arsphenamin. The tenth and each succeeding injection were followed by epistaxis and bleeding from the gums, of gradually increasing severity. After the fifteenth injection some purpuric spots appeared on the skin, which increased in severity following the last dose on December 8. Hemorrhages from the nose, gums, and vagina were now severe and the patient died three weeks later. The blood showed the following changes: Red blood cells, 1,601,000; white blood cells, 4,650 (polymorphonuclears 30 per cent., lymphocytes 25, mononuclears 35); coagulation time, nineteen minutes; bleeding time more than one hour. The clot was not retractile. The authors call attention to the blood picture, which they state resembles that of purpura and hemophilia. They believe that the damage was caused by the action of arsenic on the liver.

Eschbach³ reports a similar fatal case, following the second dose of neo-arsphenamin. The details are scanty.

Two cases are reported by Görke.⁴ Both patients were women, of whom one died and one recovered. In one instance the drugs employed were sodium arsphenamin and neo-arsphenamin; in the other, silver arsphenamin. The symptoms were the same in both cases, con-

2. Labbé, M., and Langlois, S.: *Purpura hémorrhagique aigu par intoxication arsénicale*, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:786, 1919.

3. Eschbach, H.: *Contribution au rôle du novarsénobenzol dans les ictères chez les syphilitiques et dans les dyscrasies sanguines*, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:1120, 1919.

4. Görke, H.: *Auftreten von aplastischer anämie nach Salvarsan*, München. med. Wchnschr. **67**:1226, 1920.

sisting of hematemesis, epistaxis, severe skin purpura and necrotic angina. The blood picture was similar to that described in our own case, consisting of anemia, marked leukopenia with an almost complete absence of leukoblastic bone marrow cells and decrease in platelets.

In our opinion, reactions of this type are by no means so rare as the few reports in the literature would indicate. We have shown that damage to the bone marrow, as indicated by changes in the blood picture, is also present in the majority of patients reacting to arsenical drugs, with a rash of the exfoliative dermatitis group, and that these blood changes differ only in degree from the maximally severe reaction, as seen in this case. It has been further demonstrated⁵ that the blood changes may be produced to a mild degree by the administration of an arsenical drug without the occurrence of any reaction. We, therefore, regard as closely interrelated the arsenical reactions of dermatitis exfoliativa, stomatitis, itching and purpura, the connecting link being in the similarity of the alterations in the blood.

In a previous paper¹ we laid much stress on the recognition of the prodromal symptoms of reactions of the group, and we enumerated as important the occurrence of itching, a mild macular, maculopapular or vesicular rash, prolonged fever, malaise or any tendency toward purpura. Since the preparation of this material, we have had the opportunity of observing several patients in whom such prodromes occurred. In each instance, a study of the blood revealed a slight decrease in neutrophil cells, eosinophilia from 5 to 8 per cent., a slight increase in the large mononuclear transitional group and the presence of numerous fragile leukocytes. The necessity for caution in further treatment was thus strongly emphasized.

While we have nothing to offer regarding the treatment of these reactions, the means we have suggested for their early recognition on the basis of the blood picture represents a definite step toward the prevention of the more severe forms.

SUMMARY

We present the history of a patient who developed a fatal aplastic anemia after neo-arsphenamin. The literature is reviewed, attention is drawn to the relation of this type of reaction to dermatitis exfoliativa following arsphenamin, and the practical application of early recognition of the characteristic blood changes in the prevention of these reactions is pointed out.

5. Moore, J. E.: The Action of Arsenicals on the Blood Picture in Man, *Exper. Med.*, to be published.

STUDIES CONCERNING THE INFLUENCE OF ARSENICAL PREPARATIONS ON CUTANEOUS TESTS

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For a long time the medical profession has felt the urgent need of a simple and certain diagnostic test for syphilis. The wide distribution of syphilis, the fact that syphilis can and does simulate many other diseases, and the fact that even experts are at times baffled in their diagnosis, have emphasized the necessity for a simple and certain diagnostic test for this disease.

After von Pirquet announced his reaction for tuberculosis, many investigators, among them Finger, Wolff-Eisner, Nicholas and others, attempted to obtain a specific reaction by applying extracts of syphilitic tissues to the skin of syphilitic patients. Neisser and Meirowsky had found that normal hepatic extract could not only occasionally give a similar exanthematic result as syphilitic extract, but that the test might also give a positive result in patients in whom there was no reason to suppose the existence of syphilis. In spite of some rather encouraging results, the majority of results from this method proved contradictory and disappointing. Both Neisser and von Pirquet expressed the hope and belief that a specific skin test for syphilis could be obtained by employing the extract of *Spirochaeta pallida* free from tissue constituents.

With Noguchi's cultivation of *Spirochaeta pallida*, a new stimulus was given to these investigations. In 1911, Noguchi brought out "luetin" a sterile extract of the spirochete unadulterated by any tissue constituents. Luetin was injected intracutaneously in a dose of 0.07 c.c. diluted with salt solution, or 0.035 c.c. undiluted. The skin of the arm was suggested as the site of injection. In this investigation the luetin of Parke, Davis and Company was employed. The dose was 0.07 c.c. injected intracutaneously into the upper arm. We quote from a personal letter sent us by Parke, Davis and Company which details the method they followed in manufacturing their luetin:

"Pure cultures were allowed to grow for periods of six, twelve, twenty-four and fifty days at 37 C. under anaerobic conditions. One was cultivated in ascitic fluid containing a piece of sterile placenta and the other in ascitic fluid agar also containing placenta. The lower

portion of each solid culture in which a dense growth had occurred was cut out and the tissue removed. The agar columns which contained innumerable spirochetes were then carefully ground in a sterile mortar. The resulting thick paste was gradually diluted by adding, little by little, the fluid cultures which also contained an enormous mass of the pure organisms. The dilution was continued until the emulsion became perfectly liquid. The preparation was next heated to 60 C. for sixty minutes in a water bath and then 0.5 per cent. phenol was added. When examined under a dark-field microscope, 40 to 100 dead *Spirochaeta pallida* per field could be seen."

INTERPRETATION OF REACTION

In our investigation we found that a number of our patients, after receiving luetin injections, showed a small papule devoid of erythema. This was noted twenty-four and forty-eight hours after the test was made, but disappeared subsequently. This type of reaction we considered of negative value.

Two types of positive reactions were observed: (a) Papular: This consisted of a large, red, indurated papule which made its appearance in from twenty-four to forty-eight hours after injection, usually attended with a surrounding erythema. In the great majority of our subjects this reaction disappeared at the end of a week. (b) Pustular: This type of reaction began as the papular, except that the lesions became edematous looking and at times associated with the development of miliary vesicles. The lesion soon became pustular with crusting and, at times, very slight scar formation. In several instances of this type of reaction the pustular condition persisted for three weeks before healing.

Our investigation had for its aim the determination of these facts:

1. What would be the influence of a repetition of the luetin test and the tuberculin (von Pirquet) test?
2. What would be the influence of intravenous injections of arspenamin on the luetin test and the tuberculin (von Pirquet) test?
3. What would be the influence of intravenous injections of cacodylate of soda on the luetin test and the tuberculin (von Pirquet) test?

THE INFLUENCE OF A REPETITION OF THE LUETIN TEST

For a study of this problem we selected fourteen patients from the dermatologic dispensary of the Jefferson Hospital. The patients suffered from various skin diseases, principally eczema and acne vulgaris. At least two Wassermann tests were made on each patient, both of which had to be negative before they were selected as eligible for this investigation.

Table 1 shows that in every case the first luetin test was negative, that in the repetition of the test there were three instances out of four-



A, 1 H. P.; second luetin test strongly positive -pustular type obtained after three intravenous injections of arsphenamin. The first luetin test made before the injections were given was negative.



B, 2 B. C.; strongly positive tuberculin (von Pirquet) test following four intravenous injections of arsphenamin. The lesion was about the size of a quarter of a dollar, red and edematous, and surrounded by a number of small vesicles. The first tuberculin test made before the injections were given was negative.

teen in which the previous negative reaction became positive, and these positive reactions were produced in the absence of any medication. It will also be noted that in all instances but two an interval of three weeks elapsed between the first and second tests.

At this juncture it seems proper to discuss the cause or causes of these positive luetin tests produced by repetition. Among the theories which have been advanced to explain the occurrence of a positive luetin

TABLE 1.—RESULTS OF VARIOUS TESTS

Case	Diagnosis	Number of Wassermann Tests	Result of Wassermann Tests	Result of First Luetin Test	Result of First Von Pirquet	Interval Between Tests, Weeks	Result of Second Luetin Test	Result of Second Von Pirquet Test
1. E. S.	Squamous eczema	3	All Neg.	Neg.	Neg.	3	Marked papule erythma positive	Negative
2. M. M.	Pityriasis rosea	3	All Neg.	Neg.	Neg.	3	Negative	Negative
3. S. P.	Acne vulgaris	3	All Neg.	Neg.	Neg.	3	Marked papule erythma positive	Negative
4. C. R.	Acne vulgaris	3	All Neg.	Neg.	Neg.	3	Marked papule redness positive	Negative
5. C. F.	Acne vulgaris	2	All Neg.	Neg.	Neg.	2	Negative	Negative
6. W. M.	Dermatitis	4	All Neg.	Neg.	Neg.	4	Negative	Negative
7. T. M. C.	Eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative
8. G. R.	Sycosis vulgaris	2	All Neg.	Neg.	Neg.	3	Negative	Negative
9. J. P.	Seborrhea sicca	2	All Neg.	Neg.	Neg.	3	Negative	Negative
10. G. C.	Seborrhea sicca	2	All Neg.	Neg.	Neg.	3	Negative	Negative
11. M. H. B.	Leukoplacia	3	All Neg.	Neg.	Neg.	3	Negative	Negative
12. H. S.	Squamous eczema	11	All Neg.	Neg.	Neg.	3	Negative	Positive marked swelling, redness vesiculation
13. C. A. D.	Eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative
14. A. T. P.	Papular eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative

reaction in tertiary syphilis is the alleged peculiarity of the cutis of the syphilitic at that stage of the disease which Neisser termed "Umstimmung" of the skin. Can we possibly explain our positive luetin findings produced by the repetition of the luetin test on the ground that the first inoculation of dead spirochetes sensitized the skin of subjects so that the subsequent luetin tests could be capable of producing a positive result? This would appear a logical theory and would agree with the conception of the production of a positive luetin test.

THE INFLUENCE OF INTRAVENOUS INJECTIONS OF ARSPIHENAMIN. ON THE LUETIN TEST

For this study we selected seventeen patients suffering from various skin affections: acne vulgaris, eczema, psoriasis and other conditions. At least two negative Wassermann reactions were necessary before

the patients were considered eligible for this investigation. A study of this table shows that ten patients received three injections of arsphenamin, three received four injections, two received five injections and one received two injections before the luetin test was repeated.

These injections were given at weekly intervals, the average dose being 0.4 gm. given intravenously. It will be noticed that of this series nine patients gave a positive luetin reaction on repetition, and eight responded negatively to a repetition of the luetin test.

TABLE 2.—RESULTS OF ARSPHENAMIN ON LUETIN TESTS

Case	Diagnosis	Wassermann Report	Number of Wassermann Tests	Result of First Luetin Test	Number of Arsphenamin Injections	Results of Subsequent Luetin Tests
1. B. C.	Purpura	Negative	2	Negative	5	Luetin test, papule and erythema positive
2. I. C.	Aene vulgaris	Negative	2	Negative	3	Negative
3. W. H.	Urticaria	Negative	2	Negative	5	Negative
4. K. P.	Aene vulgaris	Negative	2	Negative	4	Negative
5. F. H.	Aene vulgaris	Negative	2	Negative	5	Positive, papule and erythema
6. H. H.	Urticaria	Negative	8	Negative	3	Negative
7. R. C.	Aene mutilans	Negative	2	Negative	3	Negative
8. E. R.	Aene vulgaris	Negative	2	Negative	2	Positive, marked papule becoming pustular secondarily
9. J. D.	Pityriasis rosea	Negative	2	Negative	5	Slightly positive papule with infiltration and slight erythema
10. O. D.	Aene vulgaris	Negative	2	Negative	4	Positive, papule with erythema
11. G. L.	Aene vulgaris	Negative	9	Negative	3	Negative
12. H. L.	Furunculosis	Negative	2	Negative	3	Positive, papule with erythema
13. G. S.	Folliculitis	Negative	2	Negative	3	Slightly positive papule with slight erythema
14. H. P.	Eczema	Negative	9	Negative	3	Markedly positive pustular type of reaction, see illustrations
15. H. R.	Dermatitis herpetiformis	Negative	2	Negative	3	Negative
16. B. T.	Prurigo nodularis	Negative	2	Negative	3	Markedly positive pustular type
17. R. K.	Psoriasis	Negative	2	Negative	3	Negative

THE INFLUENCE OF CACODYLATE OF SODA, INTRAVENOUSLY ADMINISTERED, ON THE LUETIN TEST

In this series we employed five patients, who fulfilled the same requirements as those in the previous series. These patients received 10 c.c. of cacodylate of soda, intravenously, this solution containing the same amount of arsenic as 0.6 gm. of arsphenamin. It will be noted that of this series only one patient presented a slightly positive reaction. It is to be regretted that this series was small. In addition we performed the luetin test on a series of seven patients who had received from ten to twenty-one injections of cacodylate intravenously at weekly intervals. Of this series one patient presented a marked reaction of the papular type, and in the other instance the papular

reaction was positive but not marked. It is our impression that this last experiment seems to prove the influence of cacodylate of soda on the luetin test.

TABLE 3.—INFLUENCE OF CACODYLATE OF SODA ON THE LUETIN TEST

Case	Diagnosis	Wasser- mann Report	Number of Wasser- mann Tests	Result of First Luetin Test	Number of Injec- tions of Caco- dylate of Soda	Results of Subsequent Luetin Tests
1. H. N.	Lichen planus	Negative	2	Negative	2	Negative
2. A. S.	Vesicular eczema	Negative	2	Negative	4	Negative
3. E. G.	Eczema	Negative	2	Negative	3	Negative
4. T. J.	Eczema	Negative	3	Negative	3	Slightly positive, papule and redness
5. C. D.	Sycosis vulgaris	Negative	3	Negative	1	Negative

INFLUENCE OF IODIDS AND BROMIDS ON LUETIN TEST

I shall review in brief the influence of iodids and bromids on the luetin test in comparison with the influence of arsenical preparations given intravenously on the same test.

It was shown by Sherrick, and confirmed by others, that nonsyphilitic persons taking bromids or iodids at the time that this skin test is made, or while these drugs are still in the body fluids, may yield well marked nonspecific reactions which may be interpreted as positive luetin reactions. N. C. Borberg, in an exhaustive study of the mechanism of this phenomenon, concludes that the administration of iodine salts produces "Umstimmung" of the skin which is apparent by an increase of the inflammatory reaction around bacterial deposits.

We feel that our study warrants us in stating that arsenic probably produces the same susceptibility of the skin in nonsyphilitic persons, so that the administration of arsphenamin may cause the production of a positive luetin test in nonsyphilitics. In our series we have shown that while the repetition of the luetin test yielded 21 per cent. positive reactions, the arsphenamin series yielded 53 per cent. positive reactions, which is highly suggestive if not conclusive.

It is an obvious step to compare the depot of luetin in the skin with that of the spirochete depot in papules and gummas, and to regard the reaction of the arsenic and also iodine imbibed tissues around the former as a picture of what may be supposed to take place around the latter. We have therefore what we may call an unspecific Herxheimer reaction—an acute aseptic inflammation.

TUBERCULIN INVESTIGATIONS

The Influence of the Repetition of the Tuberculin Test.—In this investigation we also studied the repetition of the tuberculin (von Pirquet) method. Table 1 shows that the tuberculin test in the four-

teen subjects proved negative, while the repetition resulted in one positive result among this series of fourteen patients.

Influence of Intravenous Injections of Arsphenamin on Tuberculin Test.—We then selected another series of ten patients on whom at least two Wassermann tests had been performed and performed the tuberculin (von Pirquet) test on them. We then administered arsphenamin intravenously in a dose of 0.5 gm. at weekly intervals. After our patients had received a certain number of these injections, we again performed the tuberculin (von Pirquet) method with the results shown in Table 4.

TABLE 4.—INFLUENCE OF ARSPHENAMIN ON TUBERCULIN TESTS

Case	Diagnosis	Result of First Tuberculin Test	Number of Injections of Arsphenamin	Result of Subsequent Tuberculin Test
1. B. C.	Purpura	Negative	3	Strongly positive
2. I. C.	Aene vulgaris	Negative	5	Negative
3. Wm. H.	Urticaria	Negative	4	Negative
4. D. K.	Aene vulgaris	Negative	3	Negative
5. F. H.	Aene vulgaris	Negative	4	Weakly positive
6. H. H.	Urticaria	Negative	6	Strongly positive
7. R. C. G.	Aene mutilans	Negative	6	Negative
8. E. R.	Aene vulgaris	Negative	1	Negative
9. D. M.	Pityriasis rosea	Negative	5	Negative
10. H. R.	Dermatitis herpetiformis	Negative	6	Negative

Table 4 shows that except in one instance in which only one injection of arsphenamin was given, the number of injections of arsphenamin varied from three to six; also that of this series of ten patients, two patients showed well marked reactions with distinct swelling, erythema and miliary vesicles, this phenomenon lasting about five or six days before subsiding. In all our work the tuberculin of the H. K. Mulford Company was utilized and in each instance of the test a glycerin bouillon control was made.

The Influence of Intravenous Injections of Cacodylate of Soda on the Tuberculin Test.—In five instances we studied the effect of intravenous injections of cacodylate of soda on the tuberculin (von Pirquet) test. In one instance in which the patient had been gassed in army service, the first as well as the subsequent tuberculin test made after two intravenous injections of cacodylate of soda, proved positive. In the four other instances the first tuberculin (von Pirquet) tests were negative and the subsequent von Pirquet tests after two to four intravenous injections of cacodylate of soda also were negative. Also, without doing a preliminary tuberculin test we performed a von Pirquet test on seven patients, each of whom had received intravenous injections of cacodylate of soda varying from ten to twenty treatments, and in every case but one the tuberculin tests were negative. That one showed a weak positive von Pirquet reaction.

From this study we may conclude that arsphenamin injections are capable of sensitizing the skin to such an extent that it can change the mechanism of the tuberculin (von Pirquet) test so that a positive result can be obtained.

It would appear to us that the arsphenamin acted with the tuberculin test in the same way as the arsphenamin acted with the luetin test.

N. C. Borberg, in his study of the luetin test and the effects of the iodine preparations on it, also tested the effects of the iodine preparations on the tuberculin test, and he found that the iodids were capable of influencing the tuberculin (von Pirquet) test, producing at the point of inoculation a sort of local Herxheimer reaction; hence it would appear that arsphenamin acts in the same way as the iodids both in the luetin and tuberculin tests.

It may be possible that this "Umstimmung" of the skin produced by arsphenamin may account for the influence which Stokes found arsphenamin possesses in the treatment of various forms of tuberculosis of the skin.

In an investigation which we are conducting it appears that neither the intravenous injections of arsphenamin nor that of cacodylate of soda have any influence on the anaphylactic food tests made either by the intracutaneous or the scratch methods.

CONCLUSIONS

As a result of our studies we may conclude:

1. The repetition of a luetin test in nonsyphilitic patients is capable of producing positive luetin tests in about 21 per cent. of our subjects.
2. The intravenous administration of arsphenamin apparently stimulates the production of a luetin test in nonsyphilitic patients, and in our series we were able to produce 53 per cent. positive luetin tests following this form of intravenous specific therapy.
3. In our experience the intravenous administration of cacodylate of soda acts in the same manner as arsphenamin, only more feebly.
4. The repetition of the tuberculin (von Pirquet) test may produce a positive finding, but very infrequently, occurring only once in our series of fourteen subjects.
5. The intravenous administration of arsphenamin is capable of producing a positive tuberculin (von Pirquet) test, previously negative. This occurred in three instances in our series of ten patients.
6. The anaphylactic food test made by either the endermic or scratch method does not seem to be influenced by the intravenous administration of either arsphenamin or cacodylate of soda. Our investigation of this phase of the problem is, however, not yet complete.
7. We are now engaged in studying the effect of the arsenicals given by mouth on the luetin, tuberculin and anaphylactic food tests.

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EXPERIENCES WITH SODIUM ARSPHENAMIN (DIARSENOL)

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MINNEAPOLIS

Sodium arspenamin was introduced in the early part of 1915 and was used in large quantities in Germany. Favorable reports have been made by Dreyfus,¹ Fabry and Fischer,² Gutmann,³ Hoffmann,⁴ Loeb,⁵ Seyfarth,⁶ Wechselmann,⁷ Brandweiner,⁸ Hirsch,⁹ Schmitt,¹⁰ Ylppö¹¹ and Glombitza.¹²

LITERATURE

With the exception of one preliminary report,¹³ all of the literature on this subject is confined to the German.

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Dreyfus,¹ in 1915, reported on the results of 450 injections. He used the drug in combination with mercury in cases of cerebrospinal syphilis and obtained good results. He rarely gave over 0.45 gm.

Fabry and Fischer,² after using various doses and dilutions, decided that from 0.3 gm. to 0.6 gm. (average, 0.45 gm.) in 50 c.c. of water was the best dosage. They thought the drug could be used in more concentrated solution. They gave from three to five injections in a series at a four to five day interval. They do not report any marked reactions.

Gutmann³ gave 1,538 injections to 175 patients. The drug was dissolved in 30 c.c. freshly distilled water, independent of the dose. He started with from 0.15 gm. to 0.3 gm. and gradually increased the dosage to 0.6 gm. In a few cases he gave as high as 0.75 gm. without obtaining any reactions. In a single course the highest total amount given a man was 7.5 gm. in forty-four days, in a woman 6.5 gm. in fifty-five days and in a 6-year old child 3.3 gm. in fifty days. Injections were made at four-day intervals. He did not report any serious reactions, but noted these symptoms: (1) a rise of temperature to 38 C. in 4.4 per cent. of the cases; (2) nausea, vomiting, headache, diarrhea, occasionally; (3) no albuminuria in patients treated with sodium arspenamin; (4) the angioneurotic syndrome in two patients; (5) exanthem in ten patients (eight women and two men).

From the clinical standpoint, he found that spirochetes disappeared in twenty-four hours, and the syphilitic lesions regressed rapidly. He came to the conclusion that this drug approaches old arspenamin in its therapeutic efficiency.

Hoffmann⁴ reported the results of 1,500 injections in 242 patients. The dosage in men was from 0.45 gm. to 0.6 gm. and in women from 0.3 gm. to 0.45 gm. Injections were given at from five to seven day intervals. (The smaller doses were given only at the beginning and at the end of a long course.) The drug was dissolved in freshly distilled 0.4 per cent. saline solution in the proportion of 0.1 gm. of the drug to from 10 to 20 c.c. of the saline solution. Only two patients showed severe reactions.

Loeb⁵ found that roseola and papules disappear in one week after one injection and condylomas in two or three weeks. He treated ninety-four patients. A 5½ year old congenital syphilitic patient took 0.3 gm. without bad results. He concluded that this drug is as non-toxic as neo-arsphenamin and its therapeutic activity lies between arspenamin and neo-arsphenamin.

Seyfarth⁶ used a concentrated solution (0.45 gm. in 1 c.c. of water) without any bad effects.

RESULTS OBTAINED WITH SODIUM ARSPHENAMIN THERAPY

Patient's Number	Clinical Manifestations	Laboratory Data	Number of Injections Patient Received	Number of Injections Necessary to Remove Lesions	Wassermann Reaction After First Course	Wassermann Reaction After Second Course	Remarks
863	Chancre	Spirochetes + Wassermann +	8 (0.6 gm.) biweekly	3	Negative		
17514	Chancre.....	Spirochetes + Wassermann +	3 (0.4 gm.) 3-day interval	2	Negative	Negative after 2 months	Disappeared for 2 months after 3 injections
886	Chancre.....	Spirochetes + Wassermann +	2 courses 8 (0.4 gm.) each	2	Negative	Negative	
18250	Chancre; papular eruption.....	Wassermann +	6 (0.4 gm.) biweekly	5	Negative		
16804	Chancre.....	Spirochetes + Wassermann —	8 (0.6 gm.) weekly	3	Negative	Negative	
17314	Chancre; macular eruption.....	Wassermann +	8 (0.4 gm.) biweekly	2			
15438	Tabes.....	Blood Wassermann —	8 (0.3 gm.) biweekly	...	Negative (spinal fluid)	No change
922	Chancre.....	Spirochetes + Wassermann —	5 (0.4 gm.) biweekly	1	Negative		
921	Follicular syphilid; chancre 12 years ago	Wassermann +	5 (0.4 gm.) weekly	2	Negative		
931	Alopecia.....	Wassermann +	1 (0.6 gm.)	Disappeared after first injection
16925	Chancre; roseola.....	Spirochetes + Wassermann +	8 (0.4 gm.)	1	Negative		
596	Tabes.....	Wassermann —	8 (0.6 gm.) weekly	...	Negative	No change
818	Chancre.....	Wassermann +	8 (0.4 gm.) biweekly	2	Negative		
749	Gumma on clavicle.....	Wassermann +	2 (0.4 gm.) biweekly	...	Positive	Disappeared after second injection
16454	Chancre.....	Wassermann —	8 (0.6 gm.) biweekly	3	Negative	Negative	
16674	Chancre.....	Spirochetes +	8 (0.3 gm.) biweekly	1	Negative		
166552	Aortitis.....	Wassermann +	6 (0.4 gm.) biweekly	...	Positive	Positive	
796	Tabes.....	Blood Wassermann —	8 (0.6 gm.) weekly	...	Negative	Negative	
856	Chancre; macular eruption.....	Spirochetes + Wassermann + Spinal fluid Wassermann +, blood Wassermann —	8 (0.6 gm.) biweekly (4 times)	2	Positive	Negative	
7636	Cerebrospinal syphilis.....		8 (0.4 gm.) biweekly	...	Positive	Negative	No improvement
811	Gumma palate; perforated septum	Wassermann —	14 (0.6 gm.) weekly	Improved after first	Blood Wassermann —, spinal fluid Wassermann + Positive after 1 month's rest	Marked improvement in general health

904	Alopecia.....	Wassermann +	1 (0.6 gm.) biweekly	Gradual	Disappeared after first injection
659	Wife has syphilis; asymptomatic syphilis	Wassermann +	8 (0.6 gm.) weekly	No further report
6465	Asymptomatic syphilis.....	Wassermann +	6 (0.6 gm.) weekly	...	Positive after 6 weeks' rest	
797	Alopecia; mucus patches; macular eruption; papula on nucha	Wassermann +	7 (0.6 gm.) weekly	3	Negative	
813	Chancre.....	Wassermann —	8 (0.45 gm.) biweekly	1	Negative	Gained 10 pounds
847	Papular eruption; alopecia of eyebrows	Wassermann +	7 (0.3 gm.) biweekly	Gradual	Positive	
927	Meatal chancre; squamopapular eruption	Wassermann +	5 (0.4 gm.) biweekly	3	Negative	
917	Macular eruption.....	Wassermann +	8 (0.6 gm.) biweekly	2	Negative after 3 weeks' rest	General improvement
915	Chancre.....	Spirochetes +	4 (0.6 gm.) biweekly	2	Negative	Special note
15321	Palmar syphilid.....	Wassermann +	8 (0.45 gm.) biweekly	3	Positive after 3 weeks	Positive	
878	Chancre.....	Wassermann +	11 (0.4 gm.) biweekly	1	Negative after 3 weeks' rest	Negative	
313	Papules on penis; general macular eruption	Wassermann +	3 (0.4 gm.) biweekly	2	Negative after 12 administrations of mercury	
315	Chancre.....	Spirochetes +	2 (0.4 gm.) biweekly	1	Negative after 12 administrations of mercury	
10527	Macular eruption.....	Wassermann +	6 (0.4 gm.) biweekly	2	Negative	Left city
946	Chancre; macular eruption.....	Wassermann +	2 (0.4 gm.) biweekly	2	Negative	
857	Chancre.....	Spirochetes +	5 (0.6 gm.) biweekly	2	Negative	
814	Asymptomatic syphilis.....	Wassermann +	13 (0.6 gm.) weekly	...	Positive after 6 injections	
914	Chancre; papular eruption.....	Spirochetes +	8 (0.6 gm.) biweekly	3	Negative	Negative	
932	Chancre.....	Wassermann +	4 (0.6 gm.) biweekly	2	Negative after 12 administrations of mercury	
913	Gumma on tibia.....	Wassermann +	4 (0.4 gm.) weekly	3	Negative	
936	Chancre.....	Wassermann —	5 (0.4 gm.) biweekly	1	Negative	
780	Chancre.....	Wassermann +	8 (0.6 gm.) weekly	2	Negative after 4 weeks' rest	Positive after 10 weeks' rest	
884	Chancre.....	Spirochetes +	8 (0.4 gm.) biweekly	1	Negative	
16367	Chancre.....	Spirochetes —	7 (0.4 gm.) biweekly	7	Negative	
15955	Maculopapular eruption.....	Wassermann +	6 (0.45 gm.) biweekly	3	Negative	

RESULTS OBTAINED WITH SODIUM ARSPHENAMIN THERAPY—(Continued)

Patient's Number	Clinical Manifestations	Laboratory Data	Number of Injections Patient Received	Number of Injections Necessary to Remove Lesions	Wassermann Reaction After First Course	Wassermann Reaction After Second Course	Remarks
17002	Ulcer on tonsil; macular eruption	Wassermann +	8 (0.6 gm.) weekly	1	Positive		
17228	Chancre.....	Wassermann +	8 (0.45 gm.) biweekly	8	Positive after third injection		
17672	Chancre; macular eruption.....	Wassermann +	6 (0.6 gm.) biweekly	3	Positive (?)		
18049	Macular eruption; muco patches	Wassermann +	5 (0.6 gm.) weekly	3	Positive		
18240	Chancre on lip.....	Spirochetes +	7 (0.4 gm.) biweekly	5	Negative		
18246	Alopecia; ulcer on tongue.....	Wassermann +	6 (0.6 gm.) biweekly	5		
14738	Alopecia.....	Wassermann +	4 (0.6 gm.) biweekly	After 4th dose hair stopped falling out	Negative after 12 administrations	Negative	Left city
15669	Papular eruption.....	Wassermann —	10 (0.6 gm.) biweekly	2	Negative		
15224	Papular eruption.....	Wassermann +	7 (0.6 gm.) biweekly	1	Positive after 6 weeks' rest		
15206	Papule on tongue and lower lip	Wassermann +	12 (0.3 gm.) weekly	3	Negative after 6 weeks' rest		
14985	Pustular eruption; chancre.....	Wassermann +	8 (0.6 gm.) biweekly	1	Negative after 3 weeks' rest		
15776	Chancre.....	Wassermann —	8 (0.6 gm.) biweekly	2	Negative after 3 weeks' rest		
14856	Papule on tonsil; papule on glans	Wassermann +	5 (0.6 gm.) biweekly	2		Disappeared
15907	Chancre 2 months old.....	Wassermann +	8 (0.45 gm.) weekly	3		Disappeared
16457	Papule on forehead; muco patches	Wassermann +	3 (0.6 gm.) 3 days	Disproved after 3	Negative		Improvement not marked
159?	Interstitial keratitis; adult congenital lues	Wassermann —	4 (0.4 gm.) biweekly	4	Negative after 24 administrations of mercury	Special note
1612	General macular eruption; peristitis of frontal bone	Wassermann +	3 (0.6 gm.) in 3 days	2	Positive		Marked improvement, Left city
1614	Palmar syphilid; gumma of wrist	Wassermann —	5 (0.4 gm.) 2-day intervals	5	Negative		Marked improvement
1618	Tabes; tabetic bladder.....	Wassermann +	2 (0.4 gm.) in 2 days	Slow healing	Positive		Improved rapidly when changed to mercury treatment
1624	Serpiginous ulcerating lesion of the chest	Wassermann +	3 (0.45 gm.) in 3 days	Healing after 1st injection	Negative		
261	Chancre.....	Wassermann — Spirochetes +					

Wechselmann⁷ reported the results of 12,000 injections. He gave from 0.3 gm. to 0.45 gm. twice a week, giving a total of from forty to fifty doses, without mercury. He had only two exanthems and no other severe reactions. He found that high concentration was inadvisable.

Brandweiner⁸ reported 298 injections in 189 fresh cases. After experimenting with various doses and dilutions he recommends 20 c.c. of water independent of dosage. He gained the impression that it was somewhat more toxic than neo-arsphenamin and therapeutically equal to either of the other drugs.

Hirsch⁹ found that sodium arsphenamin is an excellent, strongly acting preparation.

Schmitt¹⁰ reported on ninety-seven injections. He found it advisable not to use over 0.45 gm., and the dose was dissolved in 10 c.c. of water. Injections were made at eight-day intervals. He obtained no cutaneous reactions and concluded that sodium arsphenamin is easier and safer to give than old arsphenamin, but no more active.

Ylppö¹¹ used the drug intravenously in congenital syphilis. He gave from 0.07 to 0.1 gm., repeating from twenty to thirty-five times; he followed the cases from nine to eighteen months and observed a lasting effect.

Glombitza¹² used sodium arsphenamin in highly concentrated solution and had no reactions worthy of note. He reported in a later communication an exanthem coming on several weeks after a course of treatment. His conclusions are in accord with those of other observers.

MODE OF ADMINISTRATION

All of the injections were made intravenously with a Luer syringe of 10 c.c. capacity. The drug was dissolved in sterile, freshly distilled water. We first used a 20 c.c. dilution irrespective of this dosage, but soon concentrated the solution to 10 c.c. without any untoward effect. We used the drug in three ways:

(a) Three moderate doses (from 0.45 to 0.6 gm.) were given at twenty-four or forty-eight hour intervals, followed by twelve mercuric salicylate (0.5 c.c.) injections.

(b) Eight moderate doses (0.45 gm.) were given at three day intervals; no mercury was used in this group.

(c) A weekly moderate dose (0.6 gm.) was given for periods varying from eight to twelve weeks. Mercury was not used in this group either.

MATERIAL

A total of 545 injections was made on sixty-six patients (twenty-two with primary syphilis, thirty with secondary syphilis, nine with tertiary syphilis, and five with neurosyphilis). In all cases the patients were ambulatory and no preliminary precautions, such as an empty

stomach, atropin injections or purge, were employed. The patient, in many instances, returned immediately to his occupation, which often was physical labor.

All of the patients showed active lesions or symptoms of syphilis when the sodium arsphenamin therapy was instituted.

REACTIONS

We encountered no severe reactions resulting from injections of sodium arsphenamin. Chills and fever following the first injection, in florid cases, were almost a constant observation. Vomiting and diarrhea occurred occasionally within the first twenty-four hours. Dizziness was noted, but we had no case of syncope or collapse. Headache was complained of by a few patients.

We saw few retarded reactions. There was no case of jaundice. Dermatitis was noted twice, once rather severe, but not severe enough to result in an exfoliative dermatitis. Two patients who gave dermal reactions to neo-arsphenamin also gave dermal reactions to minute doses of sodium arsphenamin.

Anorexia and loss of weight were not noted. Perivenous infiltration, which occurred in a few cases, caused about the same degree of pain and swelling as observed with neo-arsphenamin. (Many of these injections are made by senior students.)

There were a few cases which we deem of sufficient interest to report in detail, because they emphasize certain phases.

REPORT OF CASES

RESULTS OBTAINED WITH SODIUM ARSPHENAMIN THERAPY

CASE 780.—A man, aged 26, single, with a chancre on the shaft of the penis, enlarged lymph nodes, and a positive Wassermann reaction, received eight doses of sodium arsphenamin, 0.6 gm., at weekly intervals. He rested three weeks and the Wassermann test remained negative. He developed smallpox and was isolated for six weeks, when he returned. The Wassermann reaction had reverted to positive. We believe that had mercury been administered following the sodium arsphenamin course the Wassermann reaction would have remained negative.

CASE 915.—Another case which demonstrated the need of supplementing the sodium arsphenamin course with mercury was Case 915. A man, aged 30, presented himself with a chancre; the dark field was positive; the Wassermann reaction was negative. He received six injections of 0.6 gm. sodium arsphenamin, the first three biweekly and the next three weekly. He was out of the city for six weeks. When he returned, he had a recurrent papular eruption with a positive Wassermann reaction.

CASE 1612.—A girl, aged 18, presented a generalized macular eruption, severe throat lesions and hypertrophied papules on the vulva. The Wassermann reaction was positive. She received four injections of 0.4 gm. sodium arsphenamin at four-day intervals. She did not report for two months, when she pre-

sented herself because of a severe unilateral facial paralysis which responded to antisyphilitic treatment. The Wassermann reaction at that time was still positive.

CASE 15206.—A woman, aged 22, presented herself with papules on the tongue and lower lip, general adenitis and a positive Wassermann reaction. She received four weekly doses of 0.4 gm. of sodium arspenamin. She then rested six weeks when the Wassermann reaction was negative. She was then given a second series of six weekly doses of 0.3 gm. After the second and fifth injections she suffered from severe gastric distress. After the second gastric reaction, she was given two weeks' rest and the sixth injection was made with neo-arsphenamin (Metz), 0.3 gm. A similar reaction occurred. Mercury was ordered for subsequent treatment. This case shows that a reaction may not be due to a particular form of arspenamin.

CASE 106552.—A man, aged 32, with aortitis, had previously received twenty-six injections of neo-arsphenamin, thirty-six injections of mercury, and sixty mercury rubs. The Wassermann reaction was persistently positive. He was given six injections of sodium arspenamin, 0.4 gm., weekly. The Wassermann reaction remained positive throughout. He complained of severe gastric upset and depression throughout the course.

COMMENTS

Sodium arspenamin offers the physical and therapeutic features of arspenamin in convenient form. It is difficult, from a clinical experience, to arrive at an accurate determination of the relative value of the various arspenamins. Suffice it to say that sodium arspenamin exerts a marked effect on cutaneous and mucous membrane lesions of syphilis, and that this action is almost as rapid and profound as when arspenamin or neo-arsphenamin is employed.

The dosage employed by us was small. Marked effect was produced on lesions with 0.3 gm. given to males of approximately 150 pounds' weight. From our observations, we believe that 0.45 gm. is a safe and efficient dose, and we noted that doses of 0.6 gm., although borne without severe reactions, nevertheless produced a certain effect on the patient, which patients described as, "makes me feel sort of tired" or "I'm kind of grippy."

We used a dilution of 20 c.c. with the first doses given. This dilution was gradually and cautiously decreased to 10 c.c. No change in effect or safety of administration was noted.

We found that a course of six doses of from 0.3 gm. to 0.6 gm. made an optimum course. Injections subsequent to six doses often produced minor symptoms of intolerance (gastric distress, itching sensation).

Injections were made daily for three doses; injections were made every forty-eight hours for three doses; biweekly injections for six doses and weekly injections for six doses were made without any symptoms which we could attribute to the interval. We believe that in all arspenamin courses the patient must be carefully watched and

questioned for early warning symptoms on the part of the organism against arsenic, and that the slightest significant symptom should cause the operator to delay subsequent injections in order to avoid accumulative effect. We have not observed a case of exfoliative dermatitis which was the result of an initial dose of any of the arsphenamins. Our cases of dermatitis have occurred after repeated doses, and when we have carefully questioned the patient afterwards, we have discovered minor symptoms which we did not heed at the time, making our subsequent injection in spite of the warning, with a resulting dermatitis. We wish to call particular attention to two such minor symptoms: first, itching, which appears shortly after injection and lasts for from twelve to twenty-four hours. We have learned to accept this as a distinct warning to lengthen the period between injections and to lower the dose. Second, substernal or epigastric, dull, but persistent, pain.

Constant use of the arsphenamins breeds contempt. Operators make light of the injection; patients speak in jocular terms of their "shot"; and they exhibit a bravado when in groups at a clinic which causes them to conceal, or at least not to mention, minor symptoms. These factors cause one to overlook the gravity of the occasion and the dangers which are lurking in antisyphilitic treatments. The responsibility rests with the operator, and we believe that many of the minor and major effects of arsenic intolerance can be avoided by a carefully regulated dose and interval.

We most emphatically believe that sodium arsphenamin does not possess any qualities which permits the omission of supplemental treatment with mercury.

Sodium arsphenamin does not change a positive Wassermann reaction to negative any faster, or slower, than any of the other arsphenamins we have used. We believe that this change is to a large degree dependent on the age of infection at the time treatment is instituted and on individual response to a certain amount of therapy.

CONCLUSIONS

1. Sodium arsphenamin is a readily soluble, easily administered and safe preparation.
2. Sodium arsphenamin exerts a marked influence on clinical manifestations of syphilis.
3. We believe that courses of sodium arsphenamin should be supplemented with mercury.
4. The therapeutic efficiency is apparently equal to that of the other arsphenamins (clinically).
5. The effect on the Wassermann reaction is about on a par with that of the other arsphenamins.

A REVIEW OF THE LITERATURE AND A DISCUSSION OF SILVER ARSPHENAMIN *

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MINNEAPOLIS

Silver arsphenamin, the latest of the arsphenamin series of drugs, is now on the market, and is being used in America. There is no English literature to guide one in determining its qualities. Our communication is an effort to review the literature on silver arsphenamin and to draw conclusions therefrom.

Silver arsphenamin was suggested by Ehrlich, whose untimely death cut short his researches, which were continued by Kolle who finally elaborated silver arsphenamin. This drug was first used clinically in March, 1918.

Kolle,¹ in 1918, in the first of a series of articles, gives the following table which shows that silver arsphenamin had a more profound effect on experimental syphilis than any of the other members of the arsphenamin group. He concludes from his work that silver when combined with the arsphenamin molecule forms a combination which has a greater spirocheticidal action than other combinations with which he worked.

In his second article, published in 1919 Kolle,² discusses at length the chemical properties of the drug and concludes that silver arsphenamin acts on the syphilitic process in a two-fold manner: The arsphenamin molecule exerts its well-known spirocheticidal effect, while the presence of the silver radical seems to inhibit the growth of the spirochetes. Therefore, he says, silver arsphenamin acts in combination.

Kolle,³ in 1920, reviewed the clinical results of various observers.

*Read before The Clinical Club, Minneapolis, April 10, 1921.

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1. Kolle, W.: Experimentelle Studien zu Ehrlich's Salvarsan therapie der Spirochätenkrankheiten und über neue Salvarsanpräparate, Deutsch. med. Wehnschr. Nos. 43 and 44, p. 1177, Oct. 24, 1918 and Oct. 31, 1918.

2. Kolle, W., and Ritz, H.: Experimentelle Untersuchungen über die Wirkung des Silbers und seiner Verbindungen auf die Kaninchensyphilis, mit besonderer Berücksichtigung des Silbersalvarsans, Deutsch. med. Wehnschr. No. 18, 1919.

3. Kolle, W.: Weitere Mitteilungen über Silbersalvarsan, Deutsch. med. Wehnschr. No. 2, 1920.

Fabry,⁴ in 1918, used silver arsphenamin on 100 patients, all of whom had active clinical manifestations of syphilis. At first he hospitalized his patients, but later he used the drug on ambulatory cases. He dissolved 0.2 gm. in 5 c.c. of sterile distilled water, and later 0.3 gm. in 6 or 7 c.c. using a 10 c.c. syringe. He found that infiltration of the subcutaneous tissues with a solution of this concentration was very painful. He concluded that 0.2 or 0.3 gm. of silver arsphenamin is sufficient to cause the disappearance of spirochetes from the lesions; that sclerosae and condylomas disappear, at least as rapidly as with old arsphenamin, and that large tertiary ulcers involute with great rapidity. No bad effects were noticed. There was a slight febrile reaction in "secondary syphilis" after the first injection. He noticed urticarial reactions in some cases, which disappeared in a few days. He did not repeat injections until all signs of dermal reaction had

EFFECT OF VARIOUS DRUGS ON EXPERIMENTAL SYPHILIS

Drug	Therapeutic Dose	Spirochetes
		Disappeared After
Old Arsphenamin	0.01 gm. per kilo	72 hours
Neo-Arsphenamin	0.015 gm. per kilo	48 hours
Copper Arsphenamin	0.004 gm. per kilo	96 hours
Gold Arsphenamin	0.005 gm. per kilo	48 hours
Platinum Arsphenamin	0.005 gm. per kilo	48 hours
Silver Arsphenamin	0.004 gm. per kilo	24 hours

subsided. The Wassermann reaction did not revert to negative as quickly as one would expect from a drug whose clinical action was so rapid and intense.

In 1919, Fabry,⁵ after further extensive use of silver arsphenamin, stated that he believed it to be the most active of the arsphenamin products on clinical manifestations and for destruction of spirochetes. At the same time, the necessary dosage is decidedly smaller than that of any of the other products. In order to determine the tolerance for the drug, he employed heroic treatment using from 0.2 to 0.3 gm. at three to four day intervals, giving ten to twenty doses. Later he decided that he obtained the same clinical results with a longer interval—five to seven days. With regard to the action on the Wassermann reaction: It became negative in many cases, but in active secondary syphilis it often remained positive. For this reason, he recommended

4. Fabry, J.: Ueber die Behandlung der Syphilis mit Silbersalvarsan, Deutsch. med. Wchnschr. No. 44, p. 1216-1218, Oct. 31, 1918.

5. Fabry, J.: Ueber Behandlung der Syphilis mit Silbersalvarsan, Deutsch. med. Wchnschr., No. 49, p. 1358-60, Dec. 4, 1919.

that a few neo-arsphenamin and mercury injections be given following a course of silver arsphenamin. He reported a case of universal weeping dermatitis after two injections (0.1 and 0.2 gm.); the patient recovered promptly.

Galewsky,⁶ in 1918, gave 700 injections of silver arsphenamin to 165 patients. The injections were given after working hours on ambulatory patients. He considers silver arsphenamin a powerful drug whose therapeutic dose is one-third that of old arsphenamin, but whose toxic dose is two and one-half times as great as neo-arsphenamin. He always used it in combination with mercury, giving ten to fourteen mercury and four to eight (0.1 to 0.15 gm.) silver arsphenamin injections for the first course, and six to eight mercury and two to four silver arsphenamin injections for the subsequent courses. He gave weekly or biweekly injections, and noted no ill effects. The Wassermann reaction became negative as often and as early as with any other arsphenamin preparation.

Galewsky,⁷ in 1920, after giving 2,000 injections, decided that the best average dose for women was 0.2 gm. and for men 0.25 gm., eight to fifteen injections constituting a course. Results were more rapid than with old arsphenamin. Spirochetes could not be found from twenty-four to forty-eight hours after the first dose. Sclerosae and roseolae disappear in a few days. The Wassermann reaction becomes negative very often after three weeks or after 1.5 to 2.0 gm. of the drug have been given, and he emphatically states that it reverts to negative more rapidly than with any other arsphenamin preparation. He concludes that silver arsphenamin takes the first place in the treatment of early syphilis and in effecting abortive "cures." In the treatment of early tabes, vascular and cerebral syphilis, special care must be exercised in using silver arsphenamin. He believed that there are fewer untoward effects with silver arsphenamin than with any of the other arsenical preparations. Finally, he believes the time has come to decide definitely in which group of cases a pure arsphenamin treatment should be instituted, and whether it is not advisable to give up the combined mercury and arsphenamin courses.

Gennerich,⁸ in 1918, gave 1,000 injections of silver arsphenamin to 100 patients. Small doses, from 0.1 to 0.2 gm., were given at four day intervals until four doses had been given; then the interval was lengthened to six or seven days until the course of five to ten injections

6. Galewsky, E.: Ueber Silbersalvarsannatrium, Deutsch. med. Wchnschr. No. 48, pp. 1326-1327, Nov. 28, 1918.

7. Galewsky, E.: Zwei Jahre Silbersalvarsan-Therapie, München. med. Wchnschr. Jan. 30, 1920.

8. Gennerich: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 45, pp. 1243-1244, Nov. 7, 1918.

had been completed. He believes that the drug is the most powerful and the safest of the arsphenamin preparations, having only four minor reactions in his entire series. Furthermore, he believes that the drug is especially suitable for the abortive "cure of primary Wassermann negative cases." A patient with this type of case he treated for from two and one-half to three weeks after first excising the chancre. He thinks courses of silver arsphenamin are more efficient in fresh secondary syphilis than courses of any other arsphenamin product or than courses of arsphenamin combined with mercury.

In 1919, Gennerich⁹ again reported on the results of 3,500 injections of silver arsphenamin on 315 patients. As the war had caused a scarcity of silver arsphenamin, some of his courses had to be supplemented with injections of neo-arsphenamin. In these cases he did not give more than seven injections of neo-arsphenamin because of the danger of icterus. In 3,500 injections of silver arsphenamin, he saw only one case of mild icterus.

Hahn,¹⁰ in 1918, gave 1,000 injections of silver arsphenamin to eighty-two patients. He treated both recent and old cases of syphilis, and was in accord with the opinion of other observers that cutaneous and mucous membrane lesions disappeared rapidly. His observations on old cases of syphilis are especially interesting. He noted that in a series of Wassermann-fast cases, the reaction soon became negative and remained negative for the length of the period of observation. He reports no severe reactions, and states his hope that this drug will eliminate the need of mercury in the treatment of syphilis.

Hahn,¹¹ in 1920, reported his further observations on silver arsphenamin, having given 4,000 injections to 300 patients. He standardized his technic beginning with 0.1 gm. and gradually increasing the dosage to 0.3 gm. given biweekly, in from 10 to 20 c.c. of sterile distilled water. The Wassermann reaction always became negative after twelve injections in fresh cases and almost always in old cases. He concluded that the action of silver arsphenamin on all the manifestations of syphilis in all its stages is excellent and that it acts rapidly and with certainty.

Hugo Miller,¹² in 1918, gave 1,000 injections of silver arsphenamin to 170 patients. He thinks that silver arsphenamin sterilizes the human

9. Gennerich: Kriegserfahrungen in der Luesbehandlung, unter besonderer Berücksichtigung des Silbersalvarsans, Berl. klin. Wchnschr., p. 769, Oct. 18, 1919; No. 34, p. 803, Oct. 25, 1919.

10. Hahn, F.: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 50, pp. 1385-1386, Dec 12, 1918.

11. Hahn, F.: Silbersalvarsan in der Syphilistherapie, Deutsch. med. Wchnschr. No. 4, pp. 92-93, Jan. 22, 1920.

12. Miller, Hugo: Silbersalvarsannatrium-Behandlung der Syphilis, Deutsch. med. Wchnschr. No. 51, pp. 1415-1416, Dec. 19, 1918.

organism infected with syphilis more thoroughly than any other drug which we have. He also thinks that the effect on the Wassermann reaction is more noticeable than with neo-arsphenamin. Dermal reaction can be avoided by slow injection with great dilution.

Sellei,¹³ in 1918, observed that secondary lesions were not immediately affected, but that a few days after injection there was rapid involution. In a case of nephritis with syphilis he gave the drug without ill effects. Sellei,¹⁴ in 1920, found that dosage of 0.04, 0.06, 0.08 and 0.1 gm. gave the same results as 0.1, 0.15, 0.2 and 0.3 gm., and affected the Wassermann reaction sooner. He believes the drug is particularly suited for use in syphilis of the nervous system.

Weichbrodt,¹⁵ in 1918, used the drug in eighteen cases of paresis and tabes. He thought the drug suitable, but drew no conclusions. There was no marked effect on paresis.

Weichbrodt,¹⁶ in 1919, noted that three months after the spinal fluid had been made negative with silver arsphenamin it became positive, and he tried in vain to revert it to negative. His final conclusion was that silver arsphenamin is the drug of choice in paresis, although it gives no permanent benefit to the patient.

Hauck,¹⁷ in 1919, reported on 600 injections into sixty patients in all stages of syphilis. He started with 0.1 gm., gradually increasing the dose to 0.25 gm. for women and 0.3 gm. for men. He gave from ten to twelve doses in a course, and did not use mercury in combination. One injection of 0.1 gm. was sufficient to cause disappearance of mucous patches. The effect of a course of silver arsphenamin was particularly striking in its effect on the lymph node enlargement. The adenitis disappeared rapidly. He found definite improvement in tabes after twelve injections of 0.1 gm. There were no severe reactions, exanthems or icteri, and he concluded that silver arsphenamin is a great advance in the therapy of syphilis.

Kerl,¹⁸ in 1919, used the drug in concentrated solution, 0.1 gm. in 6 c.c. of water, and concluded that the same result can be obtained with

13. Sellei, J.: *Das Silbersalvarsan*, Deutsch. med. Wchnschr. No. 45, pp. 1247-1248, Nov. 7, 1918.

14. Sellei, J.: *Weitere Erfahrungen mit Silbersalvarsan*, Med. Klin. No. 12, Mar. 21, 1920.

15. Weichbrodt, R.: *Silbersalvarsannatrium und Sulfoxylatpräparat* (No. 1495) in *der Paralyse-therapie*, Deutsch. med. Wchnschr. No. 44, pp. 1216-1217, Oct. 31, 1918.

16. Weichbrodt, R.: *Weitere therapeutische Versuche bei Paralyse*, Deutsch. med. Wchnschr. No. 13, pp. 357-358, Mar. 27, 1919.

17. Hauck, L.: *Die Behandlung der Syphilis mit Silbersalvarsannatrium*, Med. Klin. No. 24, pp. 581-582, Jan. 15, 1919.

18. Kerl, W.: *Ueber Silbersalvarsan*, Wien. klin. Wchnschr., 1919, No. 17, pp. 446-447.

0.1 to 0.2 gm. of silver arsphenamin that one can obtain with 0.4 gm. of old arsphenamin.

Knopf and Sinn,¹⁹ in 1919, treated eighty-two patients with active manifestations. They treated fifty-nine with silver arsphenamin only; in twenty-three cases they combined its use with mercury. Their objections to the drug were:

1. It is hard to see undissolved particles.
2. It is more difficult to determine an oxidized product than in the case of lighter colored arsphenamin.
3. It is hard to see blood in the syringe when aspirating after venipuncture.

Their technic was to administer 0.1 gm. on the first day, 0.2 gm. on the third or fifth day, and after that 0.3 gm. every fourth day for ten or twelve injections. They encountered angioneurotic reactions when they used concentrated (5 to 10 c.c.) solutions. These disappeared on using 15 to 20 c.c. of dilutant and making very slow injections. They concluded that the effect on the Wassermann reaction is not as great as would be expected in view of the intense action on clinical manifestations.

Kreibich²⁰ in 1919, gave 400 injections to 100 patients, using 0.2 to 0.3 gm. in two to four doses in a course. He gave 0.2 gm. to a weak 8-year old boy twice within ten days with beneficial effect and no reaction. He used a 10 c.c. dilution, noting only mild reactions. On active lesions, 0.3 gm. of silver arsphenamin gives about the same result as 0.4 gm. of old arsphenamin. Spirochetes begin to disappear in six hours, and are all dead (in the dark field) in twenty-four hours. Considering the arsenic content, he believes silver arsphenamin is more desirable than old arsphenamin.

Sinn,²¹ in 1919, reported a fatal case of hemorrhagic encephalitis in a man 21 years of age with florid secondary syphilis, who received three doses of silver arsphenamin. The first dose consisted of 0.15 gm.; three days later he received 0.25 gm., and four days later 0.25 gm. He also received seven injections of mercury and one injection of mercury salicylate. Two days after the last silver arsphenamin injection, he became unconscious and died three and one-half days later, in spite of all efforts.

19. Knopf, W., and Sinn, O.: Ueber Silbersalvarsan nebst Bemerkungen über Konzentrierte Altsalvarsan-einspritzungen, *Deutsch. med. Wchnschr.* No. 19, pp. 517-518, May 8, 1919.

20. Kreibich, C.: Ueber Silbersalvarsannatrium, *Med. Klin.* No. 7, Feb. 16, 1919.

21. Sinn, O.: Ueber Neurorezidive nach reiner. Salvarsan und Silbersalvarsanbehandlung, *München. med. Wchnschr.* No. 43, pp. 1228-1229, Oct. 24, 1919.

Lenzmann,²² in 1919, gave 250 injections of silver arsphenamin. He used a more dilute solution than most of the observers, 0.1 to 0.25 gm. in 20 to 40 c.c. He decided that the drug was suitable for use, and was well borne and less toxic than the other members of the arsphenamin group. The technic of injection, he thought was more difficult because of the color of the solution. The action on spirochetes was rapid. The drug was well borne by children. He had had reactions in two patients which lasted for a few days; they were characterized by substernal pain and stridulous breathing and a croupous cough. Both patients recovered. Concerning the effect on the Wassermann reaction, he thought it was too early to make a definite conclusion.

Lenzmann,²³ in 1919, used silver arsphenamin in a case of aortitis, but made no special comment on its value in this type of syphilitic involvement.

Levy-Lenz,²⁴ in 1919, gave seventy injections of silver arsphenamin. He had no severe reactions. He used a concentrated solution, 0.1 gm. in 3 c.c. of sterile distilled water, and he did not believe that slow injection was essential, or that the darkness of the fluid made injection more difficult, for aspiration when the needle was paravenous gave air bubbles, and when intravenous the volume of fluid in the syringe increased.

Von Notthaft,²⁵ in 1919, thought that the drug is the equal of old arsphenamin, but insisted on dilution and slow injection using 120 c.c. of water and a gravity apparatus. He obtained angioneurotic symptoms when he used concentrated solutions. He did not think it advisable to use silver arsphenamin simultaneously with mercury. He had given silver arsphenamin steadily for a period of six months and even longer without ill effect, and he believed that the solution is stable for at least thirty minutes.

Riecke,²⁶ in 1919, reported a death occurring in a man 41 years of age, who had a ten-week old case of florid syphilis. He was otherwise normal. He received 1.3 gm. of silver arsphenamin in seven injections over a period of forty-two days. After the first injection of 0.2 gm. he had fever, chills and weakness lasting several hours. The

22. Lenzmann, R.: Ueber Erfahrungen mit Silbersalvarsannatrium, *Deutsch. med. Wchnschr.* **45**:355-357 (March 27) 1919.

23. Lenzmann, R.: Uber Aortitis luica, *Ztschr. f. ärztl. Fortbild.* No. 23, 1919.

24. Levy-Lenz: Meine Erfahrungen mit Silbersalvarsan, *Deutsch. med. Wchnschr.* **45**:1440-1441 (Dec. 25) 1919.

25. Von Notthaft: Erfahrungen mit Silbersalvarsan, *Deutsch. med. Wchnschr.* **45**:341 (Mar. 27) 1919.

26. Riecke, E.: Schwere Erscheinungen nach Silbersalvarsan in einem Falle florider Syphilis, *Med. Klin.* No. 14, pp. 329-330 (April 6) 1919.

interval was five days. Headache and exaggeration of his first symptoms followed the third and fourth injections of 0.2 gm. The fifth injection of 0.15 gm. brought forth no symptoms of intolerance, but after the sixth injection of 0.15 gm. he had a facial erythema. In spite of this warning, he received a seventh injection of 0.2 gm. ten days later, which was followed by a severe generalized dermatitis and a complicating bronchopneumonia which terminated fatally. Riecke insisted that this death was due to intoxication with silver arsphenamin and that the drug alone was at fault.

Rille and Frühwald,²⁷ in 1919, gave ninety-two patients the usual dosage and remark that the drug is well tolerated. There were no ill effects, but its action on the Wassermann reaction was irregular.

Zieler,²⁸ in 1919, reported a case of severe generalized dermatitis following an injection of silver arsphenamin.

Buschke,²⁹ in 1919, observed two neurorecidives after initial courses of silver arsphenamin.

Carl Stern,³⁰ in 1919, gave 1,000 injections to ambulatory patients. His technic was unusual in that he dissolved the drug in a small amount of water and, after venipuncture, he aspirated considerable blood allowing the solution and the blood to mix before injection. He says that Kolle advised him that addition of serum lowered the toxicity of the drug. He also gave a few intramuscular injections which were surprisingly well borne, with very little pain.

Fritz Kalberlah,³¹ in 1919, treated nine patients with multiple sclerosis with good results, which he remarks may be due to the well-known remissions in this condition.

Deutsch,³² in 1919, observed four patients with negative Wassermann reactions in whom spirochetes were found. Each was given three doses of 0.3 gm. of silver arsphenamin at four day intervals. No further treatment was administered, but they were observed each month for one year, and they had neither a clinical nor a serologic relapse. In a fifth case of primary syphilis in which the Wassermann

27. Rille, J., and Frühwald, R.: Die Behandlung der Syphilis mit Silber-salvarsannatrium, München, med. Wchnschr. No. 43, p. 1226, Oct. 24, 1919.

28. Zieler: Würsburger Aertzeabend 17 6:19, 1919. München, med. Wchnschr., No. 29, 1919.

29. Buschke: Berl. Dermat. Geo. 13 5:19; Deutsch. med. Wchnschr. 69:435, 1919.

30. Stern, C.: Die Technik der Silbersalvarsaninjektion, München, med. Wchnschr. No. 48, p. 1377, 1919.

31. Kalberlah, F.: Die Behandlung der multiple Sklerose mit Silbersalvarsannatrium, Med. Klin. No. 32, 1919.

32. Deutsch, R.: Abortivbehandlung der Syphilis mittels Silbersalvarsan, Dermat. Wchnschr. 69:1919.

reaction was positive, he gave a total of 1.2 gm. of silver arsphenamin. The Wassermann reaction promptly became negative and remained so throughout the year of observation without further treatment.

Delbanco,³³ in 1919, treated sixty ambulatory cases with good results and no marked reactions.

Hoppe,³⁴ a neurologist, in 1919, treated twenty patients with neurosyphilis. He gave both intravenous and intramuscular injections of silver arsphenamin. The intramuscular injections were not very painful, and the local reaction caused passed away rapidly for in a week neither physician nor patient could tell on which side the previous injection had been given.

Schönfeld and Birnbaum,³⁵ in 1919, reported the use of silver arsphenamin for one year on sixty-seven patients, 1,000 injections being given. They concluded that its action on clinical manifestations is rapid; that silver arsphenamin surpasses neo-arsphenamin and sodium-arsphenamin; it about equals old arsphenamin and is less toxic. Its action on lymphadenitis is remarkably swift. The effect on the serology was found to be variable. Mild reactions were more frequent with silver arsphenamin than with old arsphenamin, but prolonged reactions were not encountered. In retrospect, after a year's use, they recommend that mercury still be combined in the therapy of old syphilis.

Goldberger,³⁶ in 1919, gave 266 injections to sixty patients. He reported no bad effects, but he believes that we should persist in the combination of mercury with arsphenamin. Since silver arsphenamin is more active than neo-arsphenamin and less toxic than old arsphenamin, Goldberger thinks that the change is very desirable, but if there is the slightest warning of intolerance, it should be discontinued at once.

Bruhns and Löwenberg,³⁷ in 1919, reported the results of 1,000 injections on 107 patients. Spirochetes disappeared in sixteen hours after the injection of 0.1 gm. They summarize the results on the Wassermann reaction: "Fifty-five strongly positive cases at the beginning of the course, forty-nine were negative at completion." They

33. Delbanco, E.: Zum Silbersalvarsan und zur Biologie der Menschen und Kaninchensyphilis, *Deutsch. med. Wchnschr.* **45**:150 (Feb. 6) 1919.

34. Hoppe, J.: Ueber Silbersalvarsannatrium, *München. med. Wchnschr.* No. 48, p. 1376, 1919.

35. Schönfeld, W., and Birnbaum, G.: Ueber Silbersalvarsannatrium mit besonderer Berücksichtigung des Verhaltens der Wassermann Reaktion. *München. med. Wchnschr.* No. 38, p. 1087, Sept 19, 1919.

36. Goldberger, P.: Unsere Erfahrungen mit Silbersalvarsan, *Med. Klin.* No. 38, 1919.

37. Bruhns, C., and Löwenberg: Ueber Silbersalvarsannatrium und die Dosierung des Salvarsans nebst Mitteilung eines Falles von Encephalitis haemorrhagica nach Neosalvarsan, *Berl. klin. Wchnschr.*, 1919, No. 39, p. 913, No. 40, p. 948.

observed slight exanthems and icterus frequently, but always after repeated doses, which emphasizes the necessity of giving the larger doses at longer intervals to avoid accumulative effect.

Dreyfus,³⁸ in 1919, reported only on purely neurologic cases. He had given 691 injections to sixty-three patients. His initial dose was 0.05 gm. to test the tolerance of the patient; he gradually increased the dose to 0.25 gm. given every second or third day. In his opinion, the drug is especially valuable in early cerebrospinal syphilis, the subjective symptoms disappearing rapidly and the objective symptoms receding in two to three weeks. In the majority of cases there is distinct improvement.

Dreyfus,³⁹ in 1919, in his second communication, dilated on the various reactions. He classifies them as follows:

1. Anaphylactic—angioneurotic syndromes. This is an immediate reaction which passes off rapidly. He did not see a severe one.
2. Fever usually follows the first injection and is probably due to "endotoxin" liberation.
3. Cutaneous manifestations are urticarial or exanthematous. Dreyfus observed only six exanthems in 1,000 injections.
4. Syncope, collapse, headache, weakness, nausea and vomiting do occur, but he believes this, "shock" type of reaction is due to too large initial dosage. He has never observed any alarming or lasting symptoms following this type of reaction.
5. Icterus in his experience is negligible for he merely mentions the possibility of its occurring.
6. Thrombophlebitis—he has not seen this in his series of cases.

Nolten,⁴⁰ in 1919, reported on 500 injections in fifty cases. He experienced no difficulties and concludes that silver arsphenamin is the most energetic and least toxic antisyphilitic remedy of the present day.

Ludwig Stern-Piper,⁴¹ in 1920, reported on the use of silver arsphenamin in multiple sclerosis. He concludes that there is some improvement which is apparently not due to the ordinary remission.

Abimelich,⁴² in 1920, in a short report comments favorably on the use of the drug.

38. Dreyfus, G. L.: Silbersalvarsan bei luetischen Erkrankungen des Nervensystems, München. med. Wchnschr., No. 31, pp. 864-869, 1919.

39. Dreyfus, G. L.: Nebenwirkungen des Silbersalvarsans, Deutsch. med. Wchnschr. Nos. 47 and 48, p. 1293, Nov. 20, 1919 and Nov. 27, 1919.

40. Nolten: Silbersalvarsan, Deutsch. med. Wchnschr. No. 36, 1919.

41. Stern-Piper, Ludwig: Beiträge zur Therapie der multiplen Sklerose mit Silbersalvarsan, München. med. Wchnschr., Aug. 20, 1920.

42. Abimelich, R.: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 10, pp. 267-268, Mar. 4, 1920.

Lochte,⁴³ in 1920, in an article entitled "Argyrie nach Zwölf Silbersalvarsan Injektionen" relates a case of argyria (?) which he himself did not see. A representative of "Der Naturheilkunde" (nature healer) sent him the following case report which he thought should be published in order to warn his colleagues of the danger of argyria following injections of silver arspenamin. Lochte, however, remarks that it cannot be verified that the case was argyria. The "nature healer" sent this report to Lochte:

A female, aged 31, infected in March, 1917, received seven neo-salvarsan injections (dose and method not given). All phenomena of lues completely disappeared in eight weeks. She suffered from a relapse in January, 1920, when she first consulted the "Nature Healer," who made a diagnosis of: (1) nodular syphilide of hairy scalp, (2) gummatous periostitis of right tibia, (3) ulcerating syphilide of right arm. Since he did not treat venereal disease, she was referred to a "specialist." (He does not state whether or not the specialist was a dermatologist.) In February, 1920, she returned to the "Nature Healer" with this story: She had reported to the specialist who had given her twelve injections of silver salvarsan. The first dose of 0.2 gm. was given intramuscularly. (The interval or size of subsequent doses was not given.) Five days after the first injection she noticed jaundice which lasted fourteen days. The treatments were not discontinued because the patient felt so well. On March 2, 1920, she noticed an ashen gray discoloration of the skin which rapidly increased.

There was no further observation of the patient. Lochte brings up the question of arsenical pigmentation caused by previous treatments with neo-arsphenamin and asks "What becomes of the silver after silver arspenamin injections?"

COMMENT

After a careful survey of the literature and as a result of a limited personal use (250 ampules), we feel that we may safely state that silver arspenamin is an efficient spirocheticide, which has a pronounced effect on the visible lesions of syphilis. It is not surprising that the effect on the Wassermann reaction is variable. The effect of all of the antisyphilitic remedies is variable in their action on this phenomenon. The personal factor must be considered; and since the same person cannot receive two drugs under precisely the same circumstances (age of infection, etc.), it is impossible to make an accurate comparison. Suffice it to say that the consensus of opinion of the many observers is that in the majority of cases of fresh syphilis a positive reaction becomes negative after the first course of from six to ten injections of silver arspenamin.

43. Lochte: Argyrie nach Zwölf silbersalvarsan Injektionen, *Therap. Holb. Monatsh.* **34**:334, June 15, 1920. Since preparation of this review three American contributions have appeared.

We note that the technic of solution and injection is perplexing to some operators. Because of the brown color of the solution, it is impossible to see undissolved particles. We have found that silver arsphenamin, being a heavy salt, immediately sinks when sprinkled on the surface of its solvent. If two beakers are used, the fluid may be gently decanted from one to the other, and when no residue is left in the bottom of the first beaker, the solution is ready for injection unless one wishes to use a filter. We encountered no difficulty in seeing the blood on aspiration after venipuncture. By using a Luer syringe with a long glass nozzle, the red blood can easily be seen passing through the lumen of the nozzle. There is considerable variation in the optimum dosage. An initial dose of from 0.05 to 0.1 gm. for a person of average weight is best—with a routine dose of from 0.2 to 0.25 gm. Many of the physicians, however, used 0.3 gm. with impunity. Solution in from 10 to 20 c.c. of water appears to be the strength of solution chosen by most of the observers. We are often warned of the necessity of making slow injections, and that the more dilute the solution the less the danger from reaction. Since Kolle advised the mixture of aspirated blood with the solution in order to reduce the toxicity (a fact which he ascertained by animal experimentation), we believe it should be the accepted technic: Dissolve the necessary dose in 10 c.c. of sterile distilled water, draw into a 20 c.c. Luer syringe, make venipuncture, aspirate about 10 c.c. of blood, and reinject the entire solution slowly. We have infiltrated 1 c.c. of such solution paravenously to note the effect. It was decidedly less painful than a like amount of sodium arsphenamin, and passed off more rapidly.

There is no difficulty in detecting an oxidized product. It is necessary to make up the solution first. The perfect product makes a rather sparkling, clear, dark brown solution. A spoiled product has a dull, muddy, grayish brown appearance.

One of the distinct advantages is the absence of the characteristic, and often nauseating, garlic-like or ether-like, odor which patients detect when they are receiving the other arsphenamins intravenously. This odor has made it impossible, or at least impracticable, to administer arsphenamin to certain patients. We administered three doses of 0.1 gm. of silver arsphenamin to such a type of patient. She made no complaint, and said she could detect no odor.

The interval of choice is from four to seven days, and the number of doses in a course varies greatly.

The majority of observers are not in favor of using silver arsphenamin and mercury simultaneously. In our clinic we always complete a course of any of the arsphenamin products before beginning a course of mercury. We can see no advantage of the mixed plan of

administration, and believe that one has less control of either drug when they are given together. Furthermore, in case of ill effect, it is difficult accurately to lay the blame.

Concerning reactions: There is apparently no reaction due to silver arspnenamin which is peculiar to that drug and has not been noticed with any of the arspnenamin group, with the possible exception of argyria, which we shall discuss later.

Angioneurotic symptoms pass off rapidly. Many observers think that this type of disturbance is due to too large an initial dose, a too concentrated solution or too rapid injection. All of this may be avoided by a diluted small initial dose, slowly injected.

Fever is noted after the first injection in florid syphilis, as with other members of the arspnenamin group.

Cutaneous manifestations, if urticarial, pass off rapidly. If the manifestations are exanthematous, they are a warning of intolerance, and should be a positive indication for cessation of arspnenamin therapy, at least for a long period (three to six months); arspnenamin should be resumed only with the greatest caution. Riecke's case of death is an example—in our opinion—of not heeding a distinct warning by the organism against further arsenic. In our experience with exfoliative dermatitis following any of the arspnenamins we noticed a decided intolerance. One patient who developed a severe dermatitis after three doses of neo-arsphenamin (0.6 gm.) at weekly intervals had a decided exanthem from 0.06 gm. given four months later, with complete rest from treatment in the interim.

• Syncope, collapse, headache, weakness, nausea and vomiting is the type of reaction which we used to see frequently when we first began using the American made arspnenamins. We noted this type of reaction almost constantly after using certain control numbers. They were promptly discarded as toxic products. Possibly this type of reaction, when noted after the use of silver arspnenamin, was due to toxic chemical by-products which unavoidably occurred in early manufacture.

Icterus is a dangerous complication and requires a careful diagnosis as to cause. Is it due to the drug or to syphilis? Few observers lay much stress on the occurrence of icterus after the use of silver arspnenamin.

Thrombophlebitis was not recorded by any observer.

No authentic case of argyria has been reported! Lochte's report is unfortunate. He did not see the case himself—the case was related to him by a "nature-healer" who did not treat the woman, but who had sent her to a "specialist." She had previously received neo-arsphenamin therapy. During her course of silver arspnenamin she developed icterus, but in spite of this, the treatment was continued,

and if the dates in the report are accurate, she received twelve doses of silver arsphenamin in less than a month's time. Kolle distinctly advises against more than 2.0 gm. in one month. Von Notthaft states that he has continued a course of silver arsphenamin for over six months without ill effect. If argyria were a common danger, one should expect to hear of it in the practice of a man who believes in continuous prolonged silver arsphenamin therapy. Lochte, in his report, suggests that the woman may have had a melanosis due to arsenic, but unfortunately she was not examined by one competent to decide.

Hemorrhagic encephalitis is reported once, but does not differ from similar cases following arsphenamin treatments.

In conclusion, we must repeat that we believe silver arsphenamin is a drug which has a marked effect on the clinical manifestations of syphilis, when administered in smaller doses than is the custom with the other arsphenamins. Whether the effect is more profound and sterilization more thorough will require a longer period of observation to determine. Immediate reactions are about the same as with the other arsphenamins, and it is too early to speak with certainty of remote dangers.

One must constantly bear in mind that silver arsphenamin is a more complex salt than any of the other arsphenamins, and the physician must be on the alert for the slightest sign of intolerance. Its superiority over the other members of the group certainly is not so marked that a patient should in any way be jeopardized in order to receive this drug in preference to the other arsphenamin products.

Although the drug is highly recommended by neurologists, nothing conclusive has been published indicating a selective action on neurosyphilis. It may be that the future treatment of syphilis will call for courses of the various arsphenamin products, each having its relative chronologic position.⁴⁴

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44. In addition to the references given, the following may be of interest: Parounagian, M.: Preliminary Report of Silver Arsphenamin, *Arch. of Dermat. & Syph.* **3**:333, (March) 1921.

Goodman, Herman: Silver Arsphenamin: Personal Experiences with the German Product, *Urol. & Cutan. Rev.* **25**:128, (March) 1921.

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THE CREAM OF A YEAR AT BEIRUT

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BEIRUT, SYRIA

Beirut, despite its isolation, offers peculiar advantages for the study of dermatology. It is on "the bridge of the world"—a connecting link to the continents of Europe, Asia proper and Africa. Its coastal summers are tropical in their heat and humidity; the high mountain ranges, with a delightful climate, are close to the humid coast; and a dry plateau occupies the interior, thus giving a wide variety of climate in a small area. Again, there is a great mingling of peoples and races and customs. Further, the American University of Beirut's School of Medicine has long been recognized as a center of medical teaching in the Near East, and its dermatologic polyclinic has been the first, and for years the only one, in this part of the world. The Kasr al Ainy government medical school at Cairo and the French Jesuit Medical School at Beirut have no dermatologic department or service, and so naturally cases of dermatoses gravitate to the American University of Beirut.

The year 1920 was in some respects remarkable, especially for the number of unusual and rare cases that came under observation, and I feel it a duty to have them put down in black and white. I have called them the "cream of a year," and perhaps I may mention that the whole amount of the "milk" was 6,261 cases, divided into polyclinic cases 3,371 and private cases 2,890. The main portion of the "skimmed milk" consisted, as in all dermatologic work, of eczema, scabies and syphilis, with the impetigos and tineas crowding close. At one period during the war scabies made up about half of my cases. In these statistics there were 1134 cases of scabies, 18.1 per cent. of all, divided into 725 clinical and 408 private cases; eczema totaled 1022 cases, or 16.3 per cent.—548 in clinic and 474 private. Eczema rarely makes up 25 per cent. of the cases in Beirut. There were 340 cases of syphilis, 5.4 per cent.—184 in clinic and 156 private cases. This represents a great falling off from war times.

I shall enumerate the cases of the diseases worthy to be classed as the cream of the year.

SKIN DISEASES IN BEIRUT

There were only three cases of acne rosacea, one clinical and two private. It is not common in Syria. It is so striking that a mistake in diagnosis is hardly possible; but I did have the rare

fortune to see two cases of acne varioliformis, one clinical and one private. Actinomycosis gave one clinical case. It is about as rare here as in the United States. I had never expected to see a case of ainhum unless I journeyed to the tropics of Africa, perhaps to see my students in the Sudan; but what was my joy to see two cases of this rare disease at Beirut last year, one case in private practice and the other in the clinic. Both patients were white people. The man had lesions on his toes, the woman on her fingers. Only one case of angioma was seen in my office and one case of alopecia universalis was observed, and that at the clinic. Blastomycosis cutis is relatively common in Syria; no less than eight cases were seen, equally divided between clinic and private practice. There were eight patients with carbuncle, all but one of them in private practice. There were four cases of cheilitis exfoliativa, one clinical and three private.

I am inclined to agree with Schamberg that colloid degeneration of the skin is not so rare a disease as the textbooks would lead us to believe. My two cases last year were private ones, and they are not the first I have seen here in Syria.

There was one case of Darier's disease—a private case; and one case of defluvium unguium in private practice; there were two cases of dengue rash in the same category. We have not had a severe epidemic of dengue in several years in Syria; the sporadic cases are common in the late summer. Not every patient has the typical rash—in fact, I would say that the rash is rather exceptional.

Among the uncommon dermatoses, there were six cases of dermatitis exfoliativa, two in the clinic, and four in the office. Dermatitis herpetiformis is a common malady in Syria; there were thirty-four cases, twenty in the clinic and fourteen in private work. Two cases of dermatitis exfoliativa neonatorum were seen at the clinic, and they were both probably fatal. I had eight cases of dermatitis repens; they were all characteristic. I have found a 1 per cent. solution of potassium permanganate constantly applied to be the best remedy.

There was one case of dermatolysis that would be a fortune-maker for a dime museum. The lesion was on the back—in fact, it occupied all of the skin on the patient's back.

Of thirteen cases of elephantiasis seven patients came to the polyclinic and six to my office. The legs were involved in all. There were fourteen cases of epidermophyton, eight in the clinic and six in office practice. I believe that epithelioma is not as common in Syria as in America. There were thirteen cases, four in clinic and nine in private work. There were nine cases of erythema nodosum, seven clinical and two private. The four cases of that relatively rare fungus disease, erythrasma, were all in private practice.

I recorded four cases of fibroma and four of Fordyce's disease, in each case one in the clinic and three in private practice. There were three cases of gangrene (spontaneous), two in the clinic and one in private work. I saw one case of herpes iris lesion—granted that it is a form of erythema multiforme—yet so uncommon are the Saturnlike rings that I felt it deserves recording as a separate entity. I had the pleasure of demonstrating it to my students at my polyclinic.

I had one case that I call, for want of a better name, herpes meningiticus. The patient was in the hospital suffering from cerebrospinal meningitis, and I was called in to treat the skin lesions. They were generalized, herpetic, and unlike anything in my experience. There were fourteen cases of herpes zoster, six in the clinic and eight private cases.

Hydroa estivale is common in Syria, and it is one of my "betes noirs." There were no less than twenty-two cases of it, equally divided between public and private practice.

All three cases of ichthyosis were seen in the clinic. There were two cases of iodism in private practice.

There were seven cases of keloids—five clinical and two private cases. One developed in a lady's chest after removing a wart with monochloracetic acid. We had two patients with keratosis palmaris et plantaris, but neither patient felt that he could afford to take roentgen-ray treatment for it. Both were clinical cases.

A most curious lesion is that of lentigo circumscripta—two cases of it were seen in the clinic. It is hard for Americans to realize how Syrians hate freckles in any form. I see a great many cases of this blemish, as well as of chloasma.

There were only three cases of lepra during the year—two clinical and one private, whereas before the war I used to average about one new case of it a month. It would seem that many lepers died during the hardships and starvation of the war. Leukoderma is fairly common and yet greatly feared in Syria, for the common name for it in Arabic is "baras," which is one of the vulgar names for leprosy. Many patients fear that it is really lepra, even when most solemnly assured that it is not. Of the seventeen patients, nine came to the clinic and seven to my house. There were five cases of leukoderma et melanoderma syphilitica—three at the clinic and two I saw privately. Two patients with leukoplakia came to my office. This is another class of patients that rarely come to the clinic, as the disease is found mostly in the well-to-do, and I have difficulty in getting patients to demonstrate to my students. I have had striking results in treating the disease with balsam of Peru; it is difficult to apply, but it turns the

trick. There were fifteen cases of lupus erythematosus, six at the clinic and nine at my office. Three cases of lipoma were seen, one in the clinic and two in private practice. I have classed lupus vulgaris with tuberculosis cutis, and it will be discussed later.

There were ten cases of moluscum contagiosum, six at the clinic and four in the office. It is a curious fact that in my first nine years of practice of dermatology in Syria I did not see one case of this lesion, and I was about to publish the statement that it seemed to be absent from this part of the world—in fact, I made this statement to my class when lecturing on it—and most curiously that same day a patient with this disease appeared in my office and two more before the week was out; but in my first ten thousand cases I did not find a single little mollusk!

One clinical and one private patient had onychomycosis. Oriental button, commonly called in Syria the Aleppo button, or the papule of a year, as translated from the Arabic, before the war was rather restricted to certain cities and towns—rife in Aleppo—but during and since that terrible upheaval it has become widespread and generally endemic. I believe that the troops are largely responsible for this great scattering of the disease. Here I wish to protest at calling the lesion a “boil.” My friend, the late Dr. Stelwagon, at my request kindly cut out the term “boil,” for the lesion has only the shape of a boil to give it that name, and that shape is retained only throughout a portion of its career. True, the term “button” smacks of French nomenclature, yet it is distinctive and for a large part of the time it answers well the description. It is a “sore” only in its last stages. I have records of 193 cases of it last year, 113 were polyclinic and 80 private cases. During the past year we began treating cases by intravenous injection of tartar emetic, in addition to my method of thorough congelation with carbon dioxid snow, which I am convinced is the most rapid and best cure. I had the privilege of discovering that treatment in January, 1910, and have used it ever since, except during some months during the war when carbon dioxid gas was not to be had in the city. I expect to publish some data on this method in the near future.

A little girl came to my office with bathing suit nevus. The concomitant hypertrichosis made it a real “bathing suit.” Only one case of nevus flammeus was seen at the clinic. People are only slowly learning what can be done for this disfigurement by carbon dioxid snow. There were fifteen cases of pigmented nevus, six clinical and nine private cases; but not a single case of nevus pilosus. In fact, the Syrians admire a hairy nevus—especially on the face. The men shave all about one, but never cut the hair on the mole, but twist and curl it till it stands out from the face at great length.

Pellagra is disappearing in Syria. It was a scourge during the war, especially among the Turkish soldiers and in the hospices and orphanages for children. I saw only eight cases of it last year, seven at the clinic and one in my office.

Of the difficult forms of pemphigus, there were six cases—two of foliaceous pemphigus, one at the clinic and one at the office; two of pemphigus neonatorum, one at the clinic and one at the office; and two of pemphigus vulgaris—one at the clinic and one at the office. I find it hard to understand the controversy over pemphigus neonatorum and how it can be mistaken for syphilis or could ever be called “*impetigo contagiosa bullosa*,” as some would have us regard the disease.

I had eleven cases of pityriasis rosea of Gibert, six at the clinic and five in my consulting room. The only patients we had last year with pityriasis rubra pilaris, or lichen ruber acuminatus, came to the clinic. (I had a clinical case of it the day that I am writing this paper. But it cannot be included in last year's record!)

Our only patient with porokeratosis came to the clinic. It is the second I have seen here. The patient we had last year had the lesion on her foot. There were two cases of progressive pigmentary dermatosis (Schamberg's disease), one at the clinic and one at my office. The two patients with prurigo nodularis (making three cases in my experience) came to my consulting room. One of them gave me the rare privilege to study the disease in its incipency, and I found it indeed a most interesting study. Of psoriasis, I had three varieties: eleven cases of vulgaris at the clinic and twenty-two at my office. For the first time I saw psoriasis nigra, and had three cases of it—two at my office and one at the clinic, and the student explaining and reporting on it made the correct diagnosis, though he felt loath to report it as he realized how rare is this variety. At the clinic we had one case of psoriasis verrucosa. There were seven cases of purpura, two clinical and five private.

We saw one case of quinine erythema at the clinic and two at my office.

Only one case of sarcoma was seen; this patient came to the clinic. Only ten cases of sycosis appeared, two in the clinic and eight in private observation. This is more than I ordinarily see here. I do not understand why sycosis should be so relatively rare in this land. Staphylococci are abundant enough for other lesions.

The Syrians tattoo their hands or arms almost as commonly as sailors; but they seldom repent of it and wish the marks removed. I had only two cases of it last year. The patients came to my office and said they wished to be rid of their dermal inscriptions. Of

twenty-eight cases of tuberculosis cutis, in which I have included lupus vulgaris, twenty-five were clinical cases and only three were private cases.

Urticaria is too common to appear in this list, but I think it is worth recording that we had at the clinic one case of giant urticaria and two of hemorrhagic urticaria. The ulcer epidemicum, which invaded Syria in 1917, produced 111 cases, fifty-one were seen at the clinic and sixty at my office. The suffering was so great that, although the disease nearly always attacks the poorer classes, they would be willing to do anything to be healed. I hope later to send some notes on this disabling disease of the skin. There were five cases of xanthoma palpebrarum, one clinical and four private; and two of xanthoma tuberosum, one at the clinic and one in the office. I had the remarkable good fortune last year to have no less than six cases of xeroderma pigmentosum. Why do we not call it malignant progressive freckles? My first case of this disease I reported fourteen years ago in the *Journal of Cutaneous Diseases* in 1907, p. 473, and I have seen no more since that time until last year, when these six patients presented themselves. One was a private patient and I had him for a season in the hospital, treating his epitheliomatous growths. I hope to report his case at further length in the near future. The other five cases were clinical cases. One was a cretin, 29 years of age, with undeveloped genitals and of dwarfish stature. He declared his brother suffered from the same malady, but we have been unable to induce him to bring his brother to the clinic. The others were two brothers from the foot of Lebanon, and two sisters from a village some 1500 meters above the sea in northern Lebanon. The mother with her daughters traveled several days on foot to the hospital, dreading for the girls the cancerous fate that overtook their father. Six cases of this mysterious malady in one year I feel are more than my share!

ROENTGEN DERMATITIS AND RADIUM DERMATITIS: A COMPARISON

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It is not the purpose in this short article to discuss the detailed symptomatology of dermatitis caused by radium or that provoked by roentgen rays—the symptomatology of both is well known to practical workers in the field.

Some authors aver that in many respects there is a pronounced difference between injuries caused by radium and those caused by roentgen rays. It has been stated that radium dermatitis is less severe than roentgen dermatitis, that it heals more quickly and that it is not followed by sequelae, or that sequelae are less likely to occur. Also the fact that keratoses, subsequent to roentgen dermatitis, will yield to radium therapy much more readily than to roentgen therapy has been used as evidence in favor of a totally different action on the part of the two agents.

That there is some difference in the reaction and some difference in the action of the two agents cannot be denied, but such broad statements as those made in the foregoing are inaccurate and misleading. They give a false sense of security to the clinician who is entering the field of radium therapy.

A clinical and histopathologic study of radium dermatitis and roentgen dermatitis, together with a knowledge of the literature, necessitates the opinion that there is no essential difference between the reactions caused by the two agents.

There is, however, a difference in some details. Unfiltered radium ("soft" beta rays) will cause a reaction that is limited principally to the epidermis and papillary body. The erythema and edema may be intense and the epidermis totally destroyed. A reaction of this type, when viewed by one whose experience has been limited to roentgen dermatitis, causes profound perturbation. This is a second degree reaction, and if provoked by roentgen rays, several months would be required for complete healing, after which sequelae, such as atrophy, scarring, telangiectasia, keratoses, etc., would be likely to develop. A second degree reaction occasioned by "soft" beta rays heals quickly (in two or three weeks) and is much less likely to have sequelae. The rapidity of repair and completeness of repair is simply a question of the degree and depth of the injury. The injury to the epidermis is of no importance. If the derma has not been injured beyond repair, recovery will be rapid, complete and permanent.

This is the type of reaction provoked by the very "soft" beta rays. These rays, being extremely active ionizers, are rapid in action but they are mostly absorbed by the first few millimeters of tissue. The more penetrating beta rays reach and are absorbed by the deeper tissues, but the dose received by the deeper layers of the derma from the customary exposure with unfiltered applicators, is usually not sufficient to injure the true skin permanently.

The superficial character of reactions occasioned by very "soft" beta rays has been demonstrated not only by histopathologic investigation, but also by the fact that sequelae are uncommon and because not infrequently hair will continue to grow after second degree reactions.

It should be clearly appreciated, however, that if the penetration and the quantity of beta radiation is sufficient to injure the true skin seriously, as happens with lightly screened applicators, and at times with unscreened applicators, then the picture will be in all respects the same as that of roentgen dermatitis.

Experimentally it is possible to obtain superficial reactions with roentgen rays—2-inch spark gap with the glass wall of the tube in contact or very close to the skin—but we have never been able to duplicate with roentgen rays the extremely superficial effect obtained with very "soft" beta rays of radium.

Many clinicians, when desiring to utilize gamma rays, cover the applicator with lead, and then place the lead-covered applicator against the skin or mucosa. As is well known, the heavy elements, when acted on by roentgen rays, gamma rays and beta rays, emit a secondary radiation having definite characteristics. The secondary radiation from lead is very "soft" (slight penetration) and will effect the same type of reaction produced by very "soft" beta rays. It is this reaction that created the idea in the minds of some clinicians that there was a profound difference between the reactions effected by roentgen rays and those provoked by gamma rays of radium. All who have had experience know that "burns" from secondary radiation can be prevented by covering the lead with aluminum, glass, leather or any substance that gives rise to few or no secondary rays.

With the exceptions noted, it is our opinion that there is no material difference between the reactions occasioned by the two agents. Penetrating beta rays and gamma rays effect reactions that are histologically and clinically indistinguishable from roentgen-ray reactions. Unfiltered roentgen rays and lightly screened radium will destroy the skin, subcutaneous tissue and even the underlying muscles. Heavily filtered roentgen rays and radium, in sufficient quantity, will destroy or seriously injure tissue to a much greater depth than will lightly-

filtered radiation. This deep effect is also enhanced by distance from the source. Heavily filtered radiation applied from a distance may even cause necrosis of the subcutaneous tissues and muscles before the skin breaks down.

It will be seen from the foregoing that the detailed symptomatology depends on the conditions under which the exposure is made, but that fundamentally the reaction is the same whether produced by roentgen rays or radium. We have seen all the symptoms and all the sequelae that constitute acute, subacute and chronic roentgen dermatitis (including the so-called roentgen-ray skin) duplicated by radium.

The fact that keratoses, due to previous roentgenization, can be cured with radium more readily than with roentgen rays is not at all mysterious or confusing. Keratoses, regardless of etiology (roentgen rays, radium, sunlight, senility, etc.) are fundamentally the same. Keratoses that appear subsequent to excessive roentgenization develop years after the treatment, and they respond to the same treatment as do keratoses from other causes. The so-called roentgen-ray keratoses may be cured with properly applied roentgen-ray treatment or with adequate applications of gamma rays. We have noted no difference in efficacy in this respect between roentgen rays and gamma rays. Beta rays are the most efficacious of any type of radiation for this purpose, when properly applied. It is possible to obtain an intense beta ray effect to a depth of at least 1 cm., and this is all that is required in the treatment of keratoses. There is reason to believe that beta rays would be more efficacious than roentgen rays or gamma rays in epithelioma, if it were possible to obtain an intense effect to a depth of several centimeters without undue injury to the more superficial tissue. It is also possible that it is the secondary beta radiation evolved in tissue acted on by roentgen rays and gamma rays that produces the therapeutic result. If so, then the penetrating roentgen rays and gamma rays simply provide a source of beta radiation at various depths below the surface.

CONCLUSION

In conclusion, we repeat that there is no essential difference between the reaction provoked by radium and the reaction effected by roentgen rays. What little difference there is, is occasioned by the fact that very "soft" beta radiation produces a more superficial "burn" than do gamma rays or roentgen rays of long wave length, and that the shortest gamma rays effect much deeper destruction with correspondingly less superficial destruction than do the shortest roentgen rays, under the usual working conditions. It is becoming the practice in Germany to use a 12-inch to 14-inch spark gap and a skin-target distance of several

feet when employing roentgen rays in deep therapy. It is possible that radiation of this kind may destroy tissue to as great a depth as very short gamma rays, as the latter are used in practice at the present writing.

What we especially desire to emphasize is that no matter how radium is employed, if the quantity is sufficient, the results may be the same as those of the roentgen rays. We have seen atrophy and telangiectasia follow a single erythema dose administered with an unscreened, flat radium applicator of the varnished type.

REMEDIES FOR RHUS DERMATITIS

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Practical therapeutics may be deductive or inductive; may, that is to say, be based on some general principles which in their turn depend on the conceptions held as to disease processes and the pharmacodynamics of certain substances; or they may be merely the result of more or less discrete observations as to the curative value of such substances in certain diseased conditions. The former method in therapeutics is often spoken of as *rational*, and the latter as *empiric*.

EMPIRIC REMEDIES

In the list of remedies for rhus dermatitis of the empiric type, we may include all those remedies that do not take into account the chemical composition of the poison. Horsfield,¹ 1798, before anything regarding the chemical nature of the poison was known, listed these remedies: ashes of the leaves and wood of the poisonous rhus, soot dissolved in milk, an aqueous solution of sodium chlorid, copper sulphate, or ammonium chlorid, leaves of *Datura stramonium*, juice of *Sanguinaria canadensis*, unguentum simplex, sweet oil, and emollient cataplasms, and an ointment of 1 dram of saccharum saturni with 1 ounce of unguentum simplex. Christy² (1829) recommended topical applications of solutions of either lead acetate, ammonium chlorid or an infusion of digitalis. He advocated producing blisters above inflamed parts. He recommended *solidago canadensis*, an Indian remedy, and said its roots were chewed and part of the resultant saliva swallowed and part rubbed on the inflamed area. Dakin,³ writing also in 1829, used locally in the treatment of this disease this prescription:

	gm. or	c.c.
R Copper sulphate	4	3 i
Precipitate of red mercury.....	4	3 i
Venice turpentine	12	3 iii
Lard	30	3 i
Mix to form an ointment.		

1. Horsfield, Thomas: An Experimental Dissertation on the Rhus Vernix, R. Radicans and R. Glabrum, Inaugural Dissertation for the Degree of M.D. at the University of Pennsylvania, 1798. Also in Medical Theses of University of Pennsylvania by Charles Caldwell 1:117-163, 1805.

2. Christy, A.: An Essay on the Poisonous Qualities of Some Species of the Genus Rhus of Linnaeus, New York Med. and Phys. J., N. S. 1:21-30, 1829.

3. Dakin, R.: Remarks on the Cutaneous Affection Produced by Certain Poisonous Vegetables, Am. J. M. Sc. 4:98-100, 1829.

In 1836, Pickett ⁴ records the local application of an old Massachusetts Indian remedy of an infusion of the bruised leaves and twigs of *Diervilla canadensis* (bush honeysuckle).

In 1837, an anonymous article ⁵ appeared, in which the treatment recommended for rhus poisoning included a topical application of from 20 to 40 grains of silver nitrate to 1 ounce of water, the skin having previously been washed clean with warm water and soap. A topical application of from 10 to 20 grains of mercuric chlorid to 1 ounce of water is not considered so good as the silver nitrate. Remedies which are considered as of little or no value, whether in weak or strong solution, are: *Diervilla canadensis*, Prot. lead acetate, potassium nitrate, potassium carbonate and sodium chlorid.

Smith, ⁶ in 1851, was led to use tincture of iodine in rhus poisoning, as it had been considered beneficial in the treatment of venomous reptile bites.

In 1858, Dr. Joseph Khittel ⁷ announced that the poison of rhus toxicodendron is a volatile alkaloid. Seven years later, in 1865, Maisch ⁸ in contrast to Khittel, considered the poison a volatile organic acid, which he named toxicodendric acid. These investigations had a noticeable effect on the rational treatment of the disease; but they are cited here merely to show that old remedies continued to be used and new ones were recommended, which did not take into consideration the volatile alkaloid of Khittel nor the volatile acid of Maisch.

In 1867, Canfield ⁹ described the mode of using *Grindelia robusta* and *G. hirsutula* as antidotes for poison oak. Either the bruised fresh herb was rubbed on the affected parts or a strong decoction, made by boiling either the fresh or dried herb, was used to wash the poisoned surfaces.

Risk ¹⁰ (1871) recommended the local application of a decoction of white oak. He also cites the alum solution of Hopkins, Dunn's decoction of cottonwood leaves for internal use, and the following formulas of Bailey:

4. Pickett, N. B.: *Diervilla Canadensis*, Boston M. & S. J. **15**:380, 1836-1837.

5. *Erythema Venenosa*, Boston M. & S. J. **17**:347-350, 1837-1838.

6. Smith, T.: Observations on the Treatment of External Poisoning by Vegetable Substances, West. Lancet **12**:293-295, 1851.

7. Khittel, Joseph: Wittstein's Vierteljahresschrift f. praktische pharmacie. **7**:348, 1858.

8. Maisch, J. M.: On the Active Principle of *Rhus Toxicodendron*, Am. J. Pharm. **38**:4-12, 1865.

9. Canfield, C. A.: *Grindelia* as an Antidote to Poison Oak, Pacific M. & S. J. **9**:294-298, 1867.

10. Risk, J. B. A.: Poison Oak, Cincin. M. Repertory **4**:316-318, 1871.

	gm. or	c.c.	
R Mercuric chlorid	2		3 ss
Distilled water	90		3 iii
Add and dissolve			
Ammonium chlorid	4		3 i
Potassium nitrate	8		3 ii
Sig.: Apply thoroughly three times a day.			

Dr. James C. White¹¹ sums up the empiric treatment of the inflammation up to 1873 thus:

A great many remedies have been recommended, in both medical and botanical books, for the treatment of persons poisoned by rhus, while others of a "domestic" character are used in various parts of the country. Among the former, a solution of acetate of lead holds the most conspicuous place. Torrey, in his "Botany of New York," says one of the best applications is a solution of sugar of lead, after the use of saline cathartics. Dr. Bigelow¹² thinks the application of acetate of lead as useful as any external palliative, and that it should be used as cold as possible. Solutions of sulphate of copper and of other metallic salts have also been recommended by physicians. Among the domestic remedies, vinegar, and solutions of saleratus and carbonate of soda, are widely and highly esteemed. A decoction of Virginia snakeroot (*serpentaria*) is also supposed to possess special power over the poison. In an old copy of Bigelow's "Florula Bostoniensis," picked up in a second-hand bookstore, I find, in connection with *Rhus toxicodendron*, a marginal note by its former owners, stating that, if soft-soap be rubbed thoroughly into the hands after handling specimens, its poisonous action will be prevented. The list comprises most of the other articles recommended by writers in medical journals as "cures" for rhus poisoning, many of which are stated to be "specific," and to act "like magic." It is needless to give the detailed directions for their application: *Grindelia robusta*, *Comptonia asplenifolia*, *dulcamara* berries (in cream), *Cephalanthus occidentalis*, *Gelsemium sempervirens*, *rhamnus*, *Lactuca elongata*, *Collinsonia canadensis*, *Quercus alba* (bark), *Lindera benzoin*, *Sassafras officinale*, *Atropa belladonna*, solutions of bromin, sulphate of zinc, chlorate of potash, chlorinated soda, sulphite of sodium, alum curd, and Turkish bath.

It is always a suspicious element in therapeutics when remedies are recommended as specifics, and when the list of cures for any one disease is exceptionally long. It is not strange, therefore, that we find even nonprofessional writers remarking that "the reputed remedies are more numerous than efficacious (Torrey and Gray)."

De Witt,¹³ 1874, used the following prescription locally:

	gm. or	c.c.	
R Glycerin	60		gr. x
Tinct. iodin	15		3 ii
Carbolic acid	2		3 ss
Morphin sulphate	0.66		3 ss

11. White, J. C.: On the Action of *Rhus Venenata* and *Rhus Toxicodendron* on the Human Skin, New York M. J. **17**:225-249, 1873.

12. Bigelow, J.: Am. Medical Botany **1**:96; **3**:20, 1817-1820.

13. De Witt, W. H.: Poisoning by *Rhus Toxicodendron*, Am. J. M. Sc. N. S. **67**:116-118, 1874.

Humphrey¹⁴ in the same year recommended sponging the surface every hour with one part of zinc sulphate in twenty-four parts of water.

Morrison,¹⁵ 1874, published the following formula to be applied constantly to the affected parts:

	gm. or	c.c.
R Carbolic acid	2	fl 3 ss
Sodium sulphite	12	3 iii
Water	120	fl 3 vi

He said that he did not know that the sodium sulphite was of any use in the formula; but he knew that it would not be of much use without the phenol (carbolic acid).

An anonymous contributor¹⁶ printed, in 1875, a prescription of mercuric chlorid, 10 grains, and lime water, 5 ounces, to be used locally. This he preferred to: sodium chlorid and potassium bicarbonate, lead acetate, lead paint thinned with linseed oil, gunpowder and water, ammonia water and olive oil.

In 1876, Yandell¹⁷ recommended a dram of quinin in twelve pills, one-third to be taken each afternoon, with no local treatment. Of external applications, he considered mercuric chlorid the best.

In 1876, Bernard¹⁸ used the fluid extract of *Gelsemium semper-virens*, externally, with good results.

Brown,¹⁹ in 1878, stated that bromin was a cure for rhus poisoning when applied externally as a mixture of from 10 to 20 drops of bromin to an ounce of olive oil, petrolatum or glycerin. This was to be rubbed gently on the affected parts, three or four times a day, and especially on going to bed at night. The oil was washed off twice daily with castile soap.

The year 1879 was a popular year for rhus remedies; at least seven were published. Those authors that did not state the chemical nature of the poison were Kahler,²⁰ Osborn²¹ and Smythe.²² Kahler used for

14. Humphrey, C. H.: Sulphate of Zinc in the Treatment of Poisoning by Rhus Radicans, *Am. J. M. Sc.* **68**:160, 1874.

15. Morrison, S. W.: Poisoning by Rhus Radicans, *Phila. M. Times* **5**:629, 1874-1875.

16. Poisoning by Rhus Toxicodendron, *Med. and Surg. Reporter* **33**:306, 1875.

17. Yandell, L. P.: Poison Oak Eruption, *Louisville Med. News* **2**:32, 1876.

18. Bernard, E. H.: Poison Oak Eruption, *Louisville Med. News* **2**:91, 1876. Sumach, *Med. Rec.* **13**:320, 1878.

19. Brown, S. A.: A Remedy for the Eruption of Poison Oak, Ivy and Sumach, *Med. Rec.* **13**:320, 1878.

20. Kahler, R.: Poisoning by Rhus (Tinct. Lobelia an Antidote), *Med. Brief* **7**:22, 1879.

21. Osborn, T. C.: On Poison Vine Eruption, *Am. M. Bi-Weekly* **10**:49-50, 1879.

22. Smythe, A. G.: Rhus Poisoning, *Med. Rec.* **16**:284, 1879; *Arch. Dermat.* **4**:320, 1879.

local application a mixture of ammonia water, 1 dram and tincture of lobelia, 7 drams, every two or three hours. Osborn used locally a cloth saturated with lime water overnight, to be exchanged the next morning for a bandage saturated with oak bark decoction. Smythe applied to the affected parts soft cloths, kept wet with a saturated solution of sodium thiosulphate.

Within the decade between 1880 and 1890, published remedies and "specifics" became more numerous. Blackwood²³ (1880) secured no real benefit by the use of alkalies (ammonia, sodium and potassium), the sulphites and bisulphites, solutions of bromin, iodine, phenol, potassium permanganate, saturated infusions and tinctures of serpentaria and lobelia, stale beer and milk. The use of lime water he considered the best local treatment. Burgess²⁴ (1880) recommended the local application of a solution of lead acetate (2 drams to a pint of water) on lint covered with oiled silk. Hardaway,²⁵ in 1881, specified a formula of $\frac{1}{2}$ ounce of zinc sulphate in one pint of water for local use. In 1882, Edson,²⁶ having used gelsemium for some years with much satisfaction in pruritic troubles, believed that it might at least alleviate the pain in rhus dermatitis. He used the following formula which speedily stopped the pain:

	gm. or c.c.	
R Phenol	2	3 ss
Fluidextract of gelsemium.....	8	3 ii
Glycerin	16	3 ss
Water, sufficient to make.....	120	3 iv

Kunze²⁷ (1883) recommended local treatment with lactic acid, acetic acid or salt water and lime juice. The lactic acid idea was the result of the buttermilk remedy, the acetic acid came from Central and South America and salt water and lime juice are popular remedies for manchineel poisoning. Hinton²⁸ (1883) stated recovery follows within twenty-four hours if a strong infusion of red sassafras root is applied frequently. Leonard²⁹ (1884) gave the following list of four topical remedies:

23. Blackwood, W. R. D.: Some Thoughts on Rhus Poisoning, Phila. Med. Times **10**:618-619, 1880.

24. Burgess, T. J. W.: On the Beneficent and Toxic Effects of the Various Species of Rhus, Canad. J. M. Sc. **5**:327-334, 1880.

25. Hardaway, W. A.: Rhus Poisoning, St. Louis Cour. Med. **6**:401-402, 1881.

26. Edson, B.: Gelsemium in Rhus Poisoning, Med. Rec. **22**:121-122, 1882.

27. Kunze, R. E.: Poison Rhus, Med. Tribune **5**:111-120, 1883.

28. Hinton: Sassafras in Rhus Poisoning, Chicago Med. Rev. **7**:15, 1883.

29. Leonard, W. W.: Rhus Poisoning, Med. Chron. **3**:21-22, 1884-1885.

	gm. or	c.c.
R Tinct. lobelia	60	℥ ii
Sodium bicarbonate	4	℥ i
Water	60	℥ ii
R Sodium thiosulphate	30	℥ i
Water	500	O i
R Spirit of nitrous ether applied without dilution several times a day.		
R Bromin	2-4	℥ i
Olive oil	30	℥ i

Tate³⁰ (1885) recommended the application of copper sulphate, 2 drams in water, 8 ounces, to stop the pain and burning.

At least seven remedies were published by different authors in 1886. Of these, an anonymous author³¹ recommended an infusion of sweet fern (*Comptonia asplenifolia*) to be applied locally. Barnes³² recommended this compound to be taken internally:

	gm. or	c.c.
R Sodium phenol sulphonate.....	6	℥ iss
Fluidextract of gelsemium.....	4	℥ i
Water, sufficient to make.....	120	℥ iv

Sig.: One teaspoonful every two hours.

Brown³³ published this modification of his 1878 remedy:

	gm. or	c.c.
R Bromin	30	℥ x-xx
Olive oil or oil of sweet almond.....		℥ i

L. D. M.^{33a} gave as a remedy the following:

R Pulverized borax	℥ ii
Phenol	℥ i
Morphin sulphate	gr. x
Compound powder of acacia.....	℥ iv
Water, sufficient to make.....	℥ viii

In criticism of this mixture, he stated that phenol and borax "help to kill the poison," and the gum acacia helps to allay irritation and pruritus. Regensburger³⁴ recommended Russian baths in the treatment of *Rhus diversiloba* dermatitis.

In 1887, Baldwin³⁵ announced a remedy in phenol ointment U. S. P., and recommended as local California remedies an infusion of *Grindelia robusta*, bay berry bush, eucalyptus, and buckeye. Couch³⁶ in the same

30. Tate, W. H.: Cutaneous Poisoning with *Rhus Toxicodendron*, *Peoria M. Month.* **6**:198, 1885-1886.

31. Jour. Cutan. and Vener. Dis. **4**:160, 1886.

32. Barnes, Edwin: *Med. Rec.* 1886, pp. 157-158.

33. Brown, A.: *Med. and Surg. Reporter* **54**:762, 1886.

33^a *Rhus Diversiloba* Remedy, *Med. and Surg. Reporter* **54**:603, 1886.

34. Regensburger, A. E.: Treatment of *Rhus* Poisoning, *J. Cutan. and Vener. Dis.* **4**:244, 1886.

35. Baldwin, A. E.: A Case of Poisoning by *Rhus Toxicodendron*, *Pacific M. & S. J.* **30**:509-512, 1887.

36. Couch, L. B.: The Treatment of *Rhus* Poisoning, *Med. Rec.* **32**:486, 1887.

year recommended frequent and thorough washing with hot soapsuds, and asserted that this treatment removed the irritant.

Hawley,³⁷ in 1890, stated that the use of oil of palustre ledum 3x if administered when the eruption first appeared would cause all symptoms to disappear within forty-eight hours.

Aulde³⁸ used whitewash externally in 1890. Kite³⁹ used black mercurial lotion similarly in 1891. Other external applications recommended in 1891 were a decoction of chestnut leaves (*Castanea fagus*) by Straley,⁴⁰ thymol iodid by Levick,⁴¹ concoction of fluid extract of serpentaria (*Virginia snakeroot*) Walker.⁴²

In 1894, Cantrell⁴³ used full strength solution of chlorinated soda (Labarraque's solution) with good results in seven cases.

An anonymous author,⁴⁴ in 1895, recommended the juice or infusion of the touch-me-not (*Impatiens fulva*). Cantrell⁴⁵ recommended phenyl salicylate (salol) and Labarraque's solution. Witmer⁴⁶ in the same year published, as a topical application, lead water and opium, to be used during the acute stage with $\frac{1}{2}$ grain of mercuric chlorid internally, every three hours.

Brown⁴⁷ two years later (1897), considered a mixture of equal parts of lime water and linseed oil a good external application; and Clarke⁴⁸ recommended a solution of borax. During the same year Smith⁴⁹ recommended lime water as effective; Todd⁵⁰ prescribed black mercurial lotion; Gilpin, fluid extract of serpentaria; Cloyd⁵¹ the juice of the wild touch-me-not; Winfield,⁵² a paste of 0.5 to 1 per cent.

37. Hawley, J. W.: *Rhus Poisoning*, Med. Advance **24**:257-262, 1890.

38. Aulde, John: *Med. and Surg. Reporter* **63**:360-365, 1890.

39. Kite, J. A.: *Weekly Med. Review* **23**:12, 1891.

40. Straley, S. B.: *Weekly M. Review* **23**:166, 1891.

41. Levick, J. J.: *Med. News* **59**:105, 1891.

42. Walker, J. B.: *Poisoning by Ivy at Second Hand*, Med. News **59**:556, 1891.

43. Cantrell, J. A.: *A Treatment for Ivy Poisoning*, Phila. Polyclinic **3**:181-182, 1894.

44. *An Antidote for Poison Ivy*, Kansas M. J. **7**:633, 1895.

45. Cantrell, J. A.: *Phila. Polyclin.* **4**:99, 450, 1895.

46. Witmer, A. F.: *Mercuric Chlorid in the Treatment of Rhus Poisoning*, Phila. Polyclin. **4**:267, 1895.

47. Brown, C. A.: *Poisoning by Rhus Toxicodendron*, Med. Brief **25**:704, 1897.

48. Clarke, T. H.: *Rhus Toxicodendron Poisoning*, Med. Brief **25**:1006, 1897.

49. Smith, C. D.: *Med. Brief* **25**:1195, 1897.

50. Todd, J. D.: *Rhus Toxicodendron Poisoning*, Med. Brief **25**:696, 1897.

51. Cloyd, A. D.: *Med. Brief* **25**:916, 1897.

52. Winfield, J. M.: *Brooklyn M. J.* **11**:404, 1897.

ichthyol, with magnesium carbonate, olive oil and simple ointment; Bartley,⁵³ sodium bicarbonate or lye water; and Hunt,⁵⁴ red mercuric iodid.

Next year (1898), Frank⁵⁵ prescribed baths followed by antiseptic emulsions containing calamin, glycerin, lime-water and the like.

In 1903, Klotz⁵⁶ used one part ichthyol to three parts of water as an application for the inflamed area; Thudichum,⁵⁷ three drops of tincture of rhus to two-thirds glass of water, a teaspoonful of the mixture to be taken three times daily, and boric acid to be used as a dusting powder. Thudichum said his daughter, having used lemon juice to remove freckles, tried it for poison ivy, and a cure resulted within thirty-six hours. Pollard⁵⁸ used a decoction of California "buckbrush" leaves locally. Hughston⁵⁹ (1905) applied with unvarying success lead acetate 10 grains, mixed with spirit of nitrous ether, 1 ounce.

In 1906, Daniel⁶⁰ considered a mixture of quinin sulphate in water a *specific*, and it cured more rapidly than calomel, 16 grains mixed with 4 ounces of lime water. Milton⁶¹ believed immunity to rhus poisoning resulted from a few doses of European anacardium.

Lindley,⁶² in 1908, recommended a solution of lead acetate and tincture of deodorized opium preferable to alcohol, hydrogen peroxid, boric acid and potassium permanganate. An anonymous writer⁶³ used a calamin and lead lotion.

Ellis⁶⁴ (1910) considered the best remedy sodium bicarbonate, when used as a dusting powder and covered with lime liniment. This he believed to be better than a saturated solution of sodium thiosulphate, a saturated solution of borax, a lead and opium wash, talcum powder, phenol ointment (1-30), iodine ointment, camphorated phenol ointment, lead acetate solution, zinc sulphate solution, and thymol iodid.

RATIONAL REMEDIES

Rational topical remedies are considered as based on general therapeutic principles and more or less erroneous conceptions of the chemical

53. Bartley, E. H.: Brooklyn M. J. **11**:405, 1897.

54. Hunt, J. H.: Rhus Poisoning, Brooklyn M. J. **11**:392-406, 1897.

55. Frank, L. F.: Med. Rec. **53**:551-554, 1898.

56. Klotz, H. G.: Merck's Arch. **5**:225, 1903.

57. Thudichum, C. L.: Rhus, Skookum Chuck, Alkaloidal Clinic **10**:831-834, 1903.

58. Pollard, F.: Poison Oak, Alkaloidal Clinic **10**:599, 1903.

59. Hughston, W. L.: Poison Ivy, Med. Brief **33**:678-679, 1905.

60. Daniel, T. J.: A Specific for Rhus Poisoning, Med. World **24**:299, 1806.

61. Milton, R. L.: Med. World **24**:59-60, 1906.

62. Lindley, J. S.: Rhus Poisoning, Am. J. Dermat. **12**:342-344, 1908.

63. British M. J. **11**:545, 1910.

64. Ellis, Richard: Poison Ivy Rash, Med. Rec. **78**:160-161, 1910.

nature of the poison and its pharmacologic action. The list of these remedies seems to begin with Horsfield¹ in 1798. Owing to the incomplete chemical analyses of Khittel,⁷ in 1857, and Maisch,⁸ in 1865, by which the poison was first considered a volatile alkaloid and then a volatile organic acid, more remedies were produced. Burrill,⁶⁵ in 1882, believed the disease to be caused by a specific parasite that infests the rhus (a view supported by Hubbard⁶⁶ in 1885, and Frost,⁶⁷ in 1916), and introduced disinfectants among the list. The work of Pfaff,⁶⁸ in 1897, which resulted in the poison's being considered a nonvolatile oil, was the cause of still other remedies. Acree and Syme⁶⁹ by their discovery, in 1906, of a supposed toxic glucosid of fisetin, rhamnase and gallic acid in *R. toxicodendron* made further alterations in the list necessary. Despite the successive discoveries as to the nature and cause of rhus dermatitis, the list of remedies, instead of decreasing, increased with each successive experiment. There were physicians who until 1908 (two years after the work of Acree and Syme) still believed the active principle to be the toxicodendric acid of Maisch and others who insisted upon its being the toxicodendrol of Pfaff.

If those substances and methods which have been used to allay the pain, itching and systemic effects, as well as those that assist involution, are excluded the list of remedies is not nearly so long as those of the empiric or inductive type.

The first substance used in an attempt at rational treatment was mercuric chlorid. This was employed by Horsfield (1798) with the hope that by its corrosive action on the skin the poison would be thrown off the affected area.

The next attempt at rational treatment involved the employment of those chemicals which when added to the poison in laboratory glassware might be expected to produce nontoxic compounds. To my present knowledge, the first experimenter in this line was Maisch (1865). In this connection he says:

As remedies against it, I have tried subacetate of lead, permanganate of potassa and ammonia, the last, I believe, with the best success. Alkaline solutions were first recommended by Professor Procter, I believe, and, as my experi-

65. Burrill, T. J.: Some Vegetable Poisons, *Am. Monthly Microscop. J.* **3**: 192-196, 1882.

66. Hubbard, S.: *Rhus Toxicodendron*, *Peoria Med. Monthly* **6**:323-324, 1885-1886.

67. Frost, L. C.: Bacterial Etiology of Poison Oak Dermatitis (*Rhus Poisoning*), *Med. Rec.* **90**:1121-1123, 1916.

68. Pfaff, Franz: On the Active Principle of *Rhus Toxicodendron*, *J. Exper. Med.* **2**:181-196, 1897.

69. Acree, S. F., and Syme, W. A.: Some Constituents of the Poison Ivy Plant, *Am. Chem. J.* **36**:301-321, 1906.

ments show, they are the remedies which a priori might be expected to afford the greatest relief, just as in the case of formic acid. The eruption produced by this acid is very similar in its nature to the one produced by toxicodendric acid, and its effects yield readily to alkaline lotions. It is not unlikely that, like the formates, the toxicodendrates are without any ill effects, if applied externally. The reactions of our new acid show, likewise, the reason why permanganate of potassa, subacetate and even acetate of lead may be valuable remedies for this eruption. While the former completely decomposes it, the last named salts produce nearly insoluble precipitates with it; at least, toxicodendric appears to be stronger in its affinities than acetic acid.

Dr. James White,¹¹ writing in 1873 and again in 1887, considered the poison to be the toxicodendric acid of Maisch. With this idea in mind, he says:

We have to deal with an acid, and the antidote for an acid is an alkali, that is, provided the salts thus formed are not equally poisonous. In poisoning by oxalic acid, for instance, potash is not an antidote, because the combination formed is nearly as poisonous as the acid itself. Whether the salts formed with toxicodendric acid by ammonia, potash, and soda are likewise poisonous, Professor Maisch leaves us somewhat in doubt as the result of experiment, but speaking clinically he leads us to believe that they are not; for he says that the application of solutions of ammonia seemed to be most effective in counteracting the action of the acid. This is consistent with the popular reputation of solutions of saleratus and soda as remedies, and will explain the action of the soft-soap. These are true antidotes, but they can be of benefit only from their chemical action, and in this way.

Of the other writers who believed the poison to be the volatile toxicodendric acid of Maisch, Park,⁷⁰ in 1879, recommended the use of a camphor-chloral mixture (equal parts of each allowed to stand in the open air and liquefy); Brandt,⁷¹ in the same year, used a saturated solution of sodium thiosulphate, externally and internally, and aborted the worst cases in from twenty-four to forty-eight hours. He also used alkaline bicarbonates and lime water locally and internally with "fair success," Ward⁷² (1879) prescribed Labarraque's solution, concentrated when the skin was unbroken and diluted with from three to six parts of water when the skin surface was broken. Johnson⁷³ (1886) used externally a formula of sodium thiosulphate, 1 ounce, distilled water 8 ounces, phenol, 1.5 drams, glycerin, $\frac{1}{2}$ ounce. Internally he used potassium iodid, 2 drams, distilled water, 7 ounces, syrup, 1 ounce, a tablespoonful four times a day. Beringer⁷⁴ (1896) used granular

70. Park, R.: *Dermatitis Venenata—or Rhus Toxicodendron and Its Action*, Arch. Dermat. **5**:227-234, 1879.

71. Brandt, W. E.: *Poisoning by Rhus Radicans*, Med. Rec. **16**:46-47, 1879.

72. Ward, J. M.: *Poisoning by Rhus Radicans*, Med. Rec. **16**:117, 1879.

73. Johnson, J. B.: *Med. and Surg. Reporter* **54**:508, 1886.

74. Beringer, G. M.: *Rhus Poisoning*, Am. J. Pharm. **68**:18-20, 1896.

sodium thiosulphate 1 dram, glycerin, $\frac{1}{2}$ fluidounce, camphor water, sufficient to make 4 fluidounces; also he used hot soda baths, and as a preventive treatment washing the face and hands with a solution of hydrogen peroxid. Davis⁷⁵ (1897) considered as a remedy a warm bath for from 15 to 20 minutes at blood heat to which 4 ounces of borax had been added. The cuticle was dried and cosmolin applied. In one hour a strong solution of lead acetate, a weak ammonia water, sodium carbonate, alum curd, or a tincture of *Grindelia squarrosa* (?) was applied. Hadden⁷⁶ prescribed, in 1906, Labarraque's solution as better than alcoholic lead acetate; Conner⁷⁷ (1907) used sodium thiosulphate mixed with glycerin and phenol, or a solution of benzoic acid and solution of formaldehyd with an equal amount of saturated solution of sodium thiosulphate. He considered quinin solution of little value; and Ward⁷⁸ (1908) used as a lotion a saturated solution of aluminum acetate, or if this is not to be had, he used phenol from 2 to 4 per cent., sodium bicarbonate, sodium sulphite, lead acetate, lotion of lead and opium or black mercurial lotion.

When the poison was found to be a nonvolatile oil by Pfaff (1897), a modified method of treatment was prescribed. He recommended the precipitation of the poison with lead acetate, copper or iron. Ordinary oxidation, he says, is very slow, but may be slightly accelerated by a solution of sodium carbonate. He does not recommend the use of oxidizers, however.

Of the physicians who followed the discovery of Pfaff, Schwalbe,⁷⁹ in 1903, recommended the use of alkalies to destroy (saponify?) the oil; he accordingly prescribed a 0.1 to 0.5 per cent. solution of potassium carbonate or a 1 to 1.5 per cent. solution of ammonium chlorid. McKee⁸⁰ (1906) believed a formula consisting of alcohol 53 per cent., distilled water, 47 per cent., and lead acetate, sufficient to make a saturated solution, would give relief for from six to eight hours. Guernsey⁸¹ (1913) considered a saturated solution of magnesium sulphate best, although he also recommended the use of strong soap and water to "neutralize the acidity of the oil," a 50 per cent. alcohol solu-

75. Davis, W. T.: *Rhus Toxicodendron* Poisoning, Med. Brief **25**:938-940, 1897.

76. Hadden, A.: *Poison Ivy or Rhus Toxicodendron*, Med. Rev. of Rev. **12**:764-765, 1906.

77. Conner, J. J.: *Poisoning by Rhus Toxicodendron*, Am. J. Dermatology **11**:368, 1907.

78. Ward, R. F.: *Severe Ivy Poisoning*, New York M. J. **88**:1224-1225, 1908.

79. Schwalbe, C.: *On the Active Principle of Rhus Diversiloba* (Poison Oak), Med. Rec. **63**:855-856, 1903.

80. McKee, E. S.: *Poisoning by Rhus Toxicodendron or Rhus Radicans*, Med. Herald, N. S. **25**:98-100, 1906.

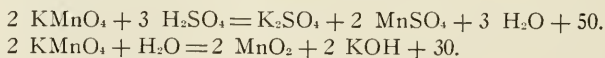
81. Guernsey, J. C.: *Rhus Poisoning*, Hahneman. Month. **48**:161-174, 1913.

tion of lead acetate, from 2 to 4 per cent. potassium permanganate, 1.5 per cent. ammonium chlorid, hydrogen peroxid, 1 teaspoonful of sodium carbonate to a quart of water, sodium thiosulphate, 1 part of household ammonia to 2 parts of water, a solution of alum, and thymol iodid or alum dusting powder.

Syme (1906) considered the poison a glucosid of rhamnose, fisetin and gallic acid. In counterdistinction to Pfaff, he recommended the use of an oxidizer, namely potassium permanganate. Syme said in part:

The best example of the latter was obtained with the ether solution from the extraction of the lead precipitate in the Soxhlet apparatus. After removing the ether, a small drop of the residue was applied to the wrist as described. An itching red spot about the size of a dime was noticed in thirty-six hours, and it steadily increased in size. Nearly two days after the application of the poison, a dilute solution of potassium permanganate containing a little caustic potash was rubbed into the spot until the pimples were destroyed. A little black spot was left wherever there had been a pimple, showing that the permanganate had been reduced to oxid in the skin. The place was washed and nothing more was thought of it until the morning following, when it was noticed that the wrist had commenced to swell during the night, and the characteristic watery secretion was running from the poisoned spot. More permanganate solution was applied without potash and the wrist was bandaged, thinking that this would prevent the spreading of the eruption, but it really facilitated spreading by becoming saturated with the poisonous fluid and keeping it in contact with a larger surface of skin. In the meantime the swelling and inflammation had extended nearly to the elbow. The arm now had the appearance of having been bitten by a snake. To reduce the swelling it was immersed in hot water. This seemed to bring out the eruption very quickly and the blisters were treated with permanganate as fast as they appeared. The swelling was reduced, but returned during the night. On the evening following, the forearm was immersed in a bowl of hot permanganate solution containing a little caustic potash. The solution was kept as hot as could be borne for about half an hour. After this bath, the poison was completely oxidized, for the swelling was reduced and did not return, nor was there any fresh eruption. What appeared to be a severe case of poisoning was thus cured very quickly. The use of hot water not only reduces the swelling, but also helps to destroy the poison. The action of permanganate is also more rapid at high temperatures.

The oxidizing power of permanganate, as is well known, is greater in acid solution than in alkaline, five atoms of oxygen being available in the former and three in the latter, according to these equations:



Permanganate was used as a remedy in some cases mixed with dilute sulphuric acid, and in others, with zinc sulphate; also with lime water. It was found to be satisfactory whether used alone or with any of the substances mentioned, provided it was well rubbed into the skin. The concentration of the solution used was varied according to the location and condition of the eruption. Where the skin was thin or already broken, dilute solutions (1 per cent.) were used. In one case, the eruption appeared in the palm of the hand

where the skin was so thick that it was necessary to open it before the remedies could reach the poison. The difficulty of getting the remedy in contact with the poison in the skin is the reason why the eruption is hard to cure.

Syme also opposed the use of an alcoholic solution of lead acetate as a remedy:

This remedy is unsatisfactory for the reason that its action consists in depositing an unstable lead compound of the poison in the skin where the conditions of moisture and temperature are favorable for its decomposition, liberating the poison with all its irritant properties. Moreover, alcoholic preparations should not be used because the alcohol dissolves the poison and, on evaporation, lets it spread over a larger surface like a varnish. Potassium permanganate, however, oxidizes the poison completely. The only objection to the use of permanganate of which the writer is aware is that it stains the skin. The stain can be removed by vigorous scrubbing with soap, or it will wear off gradually in a few days. It can be removed at once by certain acids, but these should not be used by persons not familiar with their action.

Dr. Baird⁸² on the strength of this knowledge recommended a 2 to 4 per cent. solution of permanganate in 1909.

According to my present knowledge, the next person who attempted to find an antidote through a search for a chemical neutralizer was Dr. von Adelung,⁸³ in 1912. He believed the poison to be the glucoside of Acree and Syme. His experiments in that line were as follows:

Experiment 14.—Ammonia water.—Equal parts of ammonia and tincture of rhus were mixed and tested on the skin. The mixture is toxic, from which it is evident that ammonia does not destroy the poison.

Experiment 15.—Peroxid of hydrogen.—Because it is a strong oxidizer, it was presumed that hydrogen peroxid would have some curative property. But when tested by adding it in equal quantity to the rhus tincture, it failed to inhibit the toxicity, and when tested, with control, on a patch of dermatitis it was found inert.

Experiment 16.—(Aristol.)—The left of two artificial patches of dermatitis was treated during five days with a solution of aristol in cotton-seed oil. The control received no treatment. Both were scratched. Result: The untreated patch recovered first.

Experiment 17.—The same test was made on the left of two spots produced by green leaves. The aristol in oil was applied five times in four days and protected by gauze held in place by plaster. Result: No difference could be noted. Aristol therefore appears to be of no value.

Experiment 18.—(Castor Oil.)—A mixture of equal parts of 10 per cent. tincture of rhus and castor oil was rubbed on the arm. In thirty-six hours there was a slight itching, but no eruption.

Experiment 19.—(Cedar Oil.)—A similar mixture with cedar oil was applied to the arm. After thirty-six hours, a slight eruption appeared which later developed into a fair patch of itching dermatitis.

82. Baird, A. W.: Ivy Poisoning, *Med. Rec.* **76**:232, 1909.

83. Von Adelung, Edward: An Experimental Study of Poison Oak, *Arch. Int. Med.* **11**:148-164, 1913.

Experiment 20.—(Cottonseed Oil.)—A similar mixture with cottonseed oil was applied to the thin skin of the wrist. After eight days no dermatitis had appeared.

Experiment 21.—Cottonseed oil in which green leaves had been soaked for twenty-four hours was applied to the arm. The result was slight dermatitis. This, repeated on another person, gave the same result.

Experiment 22.—Some cottonseed oil in which green leaves had been heated was applied to the arm. After four days, itching began, and in five days, a slight eruption.

Experiment 23.—A mixture of equal parts of tincture of rhus and cottonseed oil was applied to the arm. No dermatitis was detected in eight days.

These results raised the question whether cottonseed oil did not combine chemically with the toxin, destroying the toxicity. To test this point, the mixture of oil and tincture was allowed to stand a few days, when the tincture formed a layer above the oil. This supernatant fluid was toxic, producing dermatitis.

Experiment 24.—A mixture of equal parts of tincture rhus and of tincture of green soap was applied to the arm and protected by gauze. After twenty-four hours only a slight eruption was noted.

Experiment 25.—A mixture of tincture of rhus, 25 parts, and tincture of green soap, 5 parts was applied to arm and protected with gauze. Only slight dermatitis resulted.

Experiment 26.—After allowing tincture of green soap to dry on a spot, tincture of rhus was applied. A control spot was made with the rhus alone. Both spots were protected with gauze. The control took well, while the soaped spot showed a slight dermatitis. Thus it appears that soap deters the poison of rhus.

Experiment 27.—(Ichthyol Collodion.)—The worse of two patches of dermatitis, three days old, was painted with a 5 per cent. ichthyol collodion daily. In twenty-four hours, distinct improvement was noted in the treated patch, and this patch recovered earlier. This was confirmed in treating hospital cases.

Experiment 28.—(Hyposulphite of Sodium.)—Tests with this substance were also negative. It failed to inhibit the toxicity when added in large proportion to the tincture of rhus; and it failed to show curative effect on dermatitis patches compared with controls.

Experiment 29.—(Iodid of Potassium.)—This substance in strong solution, added to an equal part of tincture rhus, failed to inhibit the toxicity as tested on the skin.

Experiment 30.—(Tincture of Iodin.)—Full official strength tincture of iodine when mixed with an equal quantity of tincture of rhus destroys the poison; for when this mixture is tested on my arm no dermatitis results. If, however, the strength is reduced to less than 5 per cent. of the mixture, by addition of water or alcohol, the toxicity is not destroyed completely.

Experiment 31.—Tincture of iodine also has curative property. To one of two patches of dermatitis, official tincture of iodine was applied. The application burned. But the treated patch recovered earlier than the control. Itching quickly subsided and healing followed. The spot remained discolored and tender, presumably from iodine burning.

Experiment 32.—The right of two patches of dermatitis was rubbed with 90 drops of water mixed with 10 drops of tincture of iodine. The control was rubbed with alcohol. The application of iodine caused a burning sensation, not

severe. In twenty-four hours the rhus dermatitis had disappeared, but was replaced by an iodine burn. The control ran a normal course.

Experiment 33.—(Potassium Permanganate.)—A mixture of equal parts of potassium permanganate (0.56 gm. in 120 c.c.) with tincture rhus, when tested on the arm was found to be absolutely nontoxic.

Experiment 34.—One of two patches of dermatitis was painted with potassium permanganate in the above strength. The treated patch healed earlier than the control.

Experiment 35.—(Magnesium Sulphate.)—Chemical Tests: A fresh rhus leaf macerated with a saturated solution of magnesium sulphate remained toxic, as proven by testing on my arm.

Experiment 36.—Saturated solution of magnesium sulphate (Squibb's), added in equal quantity to tincture rhus, does not inhibit the toxicity, for dermatitis results when the mixture is applied to the skin.

Making use of the solubility of rhus poison, therapeutic experiments have been based on the remedial value of solvents as well as chemical agents. Maisch and White considered the poison soluble in water and recommended that parts exposed to rhus be immediately washed or bathed for a considerable time in water. Pfaff prescribed the mechanical removal of the poison as soon as possible after exposure by vigorously washing the affected and exposed parts with soap, water and a scrubbing brush. As the poison is soluble in alcohol, Pfaff likewise believed in thoroughly washing with alcohol and a scrubbing brush, or in washing the exposed parts with an alcoholic solution of lead acetate. He also recommended the use of oils, including petrolatum, if quickly removed and repeatedly used so as not to spread the poison. Syme, as previously quoted, believed the poison would be spread by the use of alcoholic lead acetate. Stevens⁸⁴ (1906) obtained the best results by rubbing the surface with a little petrolatum, which he scraped off with a knife, and washing the surface with a weak solution of sodium hydroxid or carbonate. He also recommended alcohol, petroleum benzin, ether or kerosene as washes to remove the poison. As heretofore quoted, von Adelung experimented with castor, cedar and cottonseed oils.

In the belief that the poison was Pfaff's toxicodendrol, Balch⁸⁵ (1906) said:

The use of soap and water and a good hand brush is the simplest method of getting rid of the oil. The action is entirely mechanical and is perfectly efficient. Alcohol dissolves and removes the oil, but successive portions must be allowed to flow over the part as after contact the alcohol may contain sufficient oil to spread the irritation. Ordinary alcohol must be used and not 50 per cent. alcohol as the latter does not dissolve the oil. The action is purely a solvent one and not one of neutralization.

84. Stevens, A. B.: Japanese Lac, Inaugural Dissertation, Ann Arbor, Mich., 1906.

85. Balch, A. W.: Poison Ivy, J. A. M. A. **46**:819-820, 1906.

Guernsey (1913), also a follower of Pfaff, recommended the use of a wash of alcohol, whisky or ether to remove the poison.

Many physicians have made clinical comparisons of various popular remedies, with or without taking into consideration the chemistry of the poison. Such comparisons of remedies, which were made successively on the same patient and therefore in different stages of the disease, are considered untrustworthy and are therefore eliminated. The earliest of these comparisons is that of Dr. Bigelow¹² (1820). He says:

The acetate of lead is perhaps as useful as any external palliative, and it should be used in solution rather than in the ointment, that it may be applied as cold as possible. The late Dr. Barton speaks highly of a solution of corrosive sublimate externally applied in this disease, but from trials of the two remedies made at the same time and in the same patient, I have found the lead the more beneficial of the two.

Cantrell⁸⁶ (1898), who carried his experiments over a long period of time and who had an abundant opportunity for experimental work, summed up the relative values of certain drugs in the treatment of ivy poisoning in order of preference, as follows: First, Labarraque's solution (dilute in erythematous and concentrated in vesicular); second, phenyl salicylate (salol) 0.5 dram to the ounce of petrolatum liquefied or ether, because both produce a cure in less than a week's time; third, bromin (10 grains to the ounce of some oily substance) cures in about ten days; fourth, boric acid (saturated or dilute solution) cures in about two weeks; fifth, acetanilid ($\frac{1}{2}$ dram to 1 dram to the ounce of liquid petrolatum) cures in about two or three weeks, because they may be relied on to produce no ill effects; sixth, *Grindelia robusta* (fluid extract 2 drams to the pint of water, more concentrated irritates), cures in about two weeks. This can always be relied on to produce a cure, but it is long delayed and may if not watched carefully produce a higher grade of inflammation.

Von Adelung in 1912 carried on comparative therapeutic tests as follows:

Though magnesium sulphate fails to destroy the toxicity of rhus when mixed with its tincture, or its juice, it, nevertheless, possesses definite therapeutic value.

Experiment 37.—Test 1: In one of two patches of dermatitis, saturated solution of magnesium sulphate was rubbed three times at hour intervals. By the next morning the treated patch was better than the control. Three more similar applications were made during the forenoon and by noon a very marked improvement was noted. The treated patch recovered earlier than the control.

86. Cantrell, J. A.: Relative Value of Certain Drugs in the Treatment of Ivy Poisoning, New England M. Monthly **17**:270-272, 1898.

Test 2.—To one of two patches of dermatitis, saturated solution of magnesium sulphate (Squibb's) was applied on gauze, covered with rubber tissue, and a bandage. A similar dressing was applied to the control, using water in place of magnesium. After twenty-four hours, while the first patch was not healed, it was free from itching, was not tender, and not edematous, thus contrasting with the control, which remained tender for six days.

HOSPITAL CASES

A. B., male, aged 23, was poisoned four days previously. Whole face was edematous and the right eye closed. On Oct. 25, 1911, in the afternoon, hot applications of 2 per cent. permanganate were begun, but applied only to the right side of the face. In thirty hours the right eye was in good condition. The left side recovered tardily.

B. C., male, March, 1912, face and hands severely poisoned. The right side of the face and the right arm were treated with the hot permanganate, while the opposite side was treated with hot standard photographer's solution of sodium hyposulphite. In addition, both arms were bandaged in their respective solutions. After twenty-four hours the patient stated that the permanganate side felt distinctly better than the other. The right side recovered the earlier.

E. U., male, aged 25, was poisoned four days previously. Both arms showed marked edema, vesicles and pustules. He had already applied cold permanganate six or seven times. Hot permanganate was applied frequently by the nurse. There was no improvement in forty-eight hours. When the solution was changed to hot mercuric chlorid, and bandaging begun with the same, recovery began.

This case illustrates the uselessness of permanganate when the vesicles become infected.

A. E., male, aged 45. Dermatitis one day old. The whole face was swollen. The eyes half closed by edema of both lids. The right ear was much swollen. Thirty hours after the dermatitis began, hot permanganate saturated solution was applied to all areas. The application burned severely, especially the eyelids. Recovery occurred in five days, though this man had always been two weeks getting well. A weaker solution of permanganate would have been better.

Besides the results of Bigelow, Cantrell and von Adelung little can be attempted in summarizing the comparative values of these remedies as the results obtained by different physicians with the same remedy are so often conflicting.

One of the chief reasons for this unsatisfactory condition is the fact that many physicians in treating a case of rhus dermatitis will first use a so-called remedy for a few applications; failing to secure a satisfactory result this remedy will be replaced by another. This process may continue until finally convalescence, delayed or accelerated by the use of the various remedies, occurs and the remedy used in the last stages of the disease is considered the best. This remedy may then be used by another physician or the same physician in the initial stages of another case with failure as a result. A condition of disputation and uncertainty

results. In support of this explanation there are the published cases of Bartlett ⁸⁷ (1838), French ⁸⁸ (1903), Matheson ⁸⁹ (1874), Morris ⁹⁰ (1897), and Stone ⁹¹ (1874).

A further discussion of remedies will be taken up in a paper on the chemotherapy of rhus dermatitis.

87. Bartlett, E.: Use of Chloride of Soda in Cases of Poisoning with Rhus Radicans, Boston M. & S. J. **18**:303, 1838.

88. French, J. M.: Rhus Toxicodendron and Rhus Poisoning, Merck's Arch. **5**:223-225, 359, 1903.

89. Matheson, A. C.: Treatment of Poisoning by Rhus Toxicodendron with Linseed Oil and Lime Water, Am. J. M. Sc., N. S. **67**:118, 1874.

90. Morris, E. K.: Guaiacol in Rhus Poisoning, Med. News **70**:57, 1897.

91. Stone, I. S.: Poisoning by Rhus Toxicodendron, Am. J. M. Sc., N. S. **67**:569, 1874.

CORRECTION

In the article by Dr. Robert S. Hodges on "Ringworm of the Nails," which appeared on page 1 of the July issue, on page 25, line 4 should read "attacking the nails."

Editorial

THE DERMATOLOGICAL RESEARCH INSTITUTE

News comes that the Dermatological Research Laboratories is hereafter to be called the Dermatological Research Institute. This change in name is probably an expression of the realization of ambitions to make this a permanent institution of research in dermatology, and the change in name has been accompanied by an act of honorable scientific altruism that is worthy of comment.

Dermatologists, and a few others perhaps, are familiar with the story of the Dermatological Research Laboratories. It was founded and supported for a few years by a rich benefactor for the purpose of making researches in psoriasis. In this work it developed a scientific staff which was capable of producing arsphenamin. When the war came on and the German supply failed us, this laboratory was able to supply the deficiency, and it was not only able to keep us from getting out of this drug, but to supply a better quality than we had had, and at a lower price. It did more than this: it was able to stabilize the situation after we got into the war, and to establish a price for this article, and a standard of quality, which probably we would have been unable to obtain had this institution not existed. Since the war it has been one of the producers of this drug, and has been foremost in the activities for its improvement.

Incidentally, in this course it has made money, and it is on its action in connection with this accumulation of money that we feel comment should be made here. This surplus amounted to the very large sum of \$511,000.00—over half a million dollars. Legally it was the property of Dr. Jay F. Schamberg, Dr. George W. Raiziss and Dr. John A. Kolmer. At a meeting of the directors of the Dermatological Research Laboratories, March 3, 1921, Dr. Schamberg, Dr. Raiziss and Dr. Kolmer transferred this sum to the Dermatological Research Institute for, to use their expression, "the common good"; which evidently means for the support of this institution of dermatologic research. At no time in the history of the laboratory has there been any division of profits among these men in any form whatever. They received salaries, and the highest one, which did not go to the director, was less than the recipient could have earned elsewhere.

An act so handsome speaks for itself, and we shall not attempt to express our admiration for it. The Dermatological Research Institute deserves a long and useful existence.

W. A. P.

Abstracts from Current Literature

SILVER SALVARSAN IN TREATMENT OF SYPHILIS. C. M. WALSON.
Am. J. Med. Sc. **161**:418 (March) 1921.

This is a report on work done with this preparation by the American Army Medical Corps in Germany. A review of the drug and its properties is given with the statement that its effect on the spirochete and its manifestations is slower with all silver salts than with neo-arsphenamin but the silver salts are less toxic and can be employed in larger doses. By animal experimentation the effectiveness of silver arsphenamin (silver salvarsan) is twice that of arsphenamin and three times that of neo-arsphenamin, the silver salt being arsphenamin plus silver, 0.25 gm. of the latter equaling 0.4 gm. of the old arsphenamin.

Emphasis is laid on having the solution well diluted, 0.1 gm. of the drug to 10 or 20 c.c. of doubly distilled water at room temperature, the injection taking at least two or three minutes. Great care should be used to prevent contact of the solution with the tissues.

Dosage will vary from 0.05 gm. to 0.1 gm. in initial doses up to 0.25 to 0.3 gm. toward the end of a course, injections being made every four days for six or eight doses. No more than 2 gm. should be given in one month.

The course of treatment recommended for the cure of syphilis consisted of four courses of silver arsphenamin and mercurial oil (the manufacturers state that mercury may not be necessary). One month is allowed to elapse between the first and second courses, each of seven doses, two and one-half months between the second and third, three months between the third and fourth.

In a series of 133 primary cases in which the lesion had existed from one to thirty days, 62 per cent. always gave a negative Wassermann reaction. Thirty-eight per cent. developed from a mild to a ++ reaction during the course of treatment. In a series of sixty-one cases of secondary syphilis all patients gave a negative Wassermann reaction after the first and second course of treatment.

The question of the use of mercury and silver arsphenamin together is not yet definitely decided, as some observers state that the two should not be used at the same time as the mercury may do harm and is superfluous, while others claim that they should be used conjointly as the mercury does no damage. All observers agree that the action of silver arsphenamin on lesions and spirochetes is prompt, and may be even more rapid than the action of arsphenamin, and that the effect of the drug is favorable in all grades of syphilis.

There is the possibility of anaphylactoid and angioneurotic symptoms in treatment with silver arsphenamin, but this could be avoided in general by the use of a small dose at the beginning of each course of treatment.

In a series of over 6,000 injections of silver arsphenamin, only two patients had arsenical poisoning which could be attributed to silver arsphenamin.

Albuminuria is not mentioned in cases in which silver arsphenamin alone was used, but it is possible that it may occur.

In general, some observers assert that silver arsphenamin is better than any other arsphenamin; some think it equal in value; while others think it produces no better results or even may prefer old arsphenamin to the new preparation.

It has not been proved that silver arsphenamin is better than arsphenamin, or that its use will replace arsphenamin and mercury in the treatment of syphilis.

JAMIESON, Detroit.

BENIGN GASTRIC ULCER IN A KNOWN SYPHILITIC. A RÉSUMÉ OF THE LITERATURE CONCERNING THE DIAGNOSIS OF ORGANIC GASTRIC SYPHILIS. W. FRANK FOWLER, Surg., Gyn. & Obst. 32:419, 1921.

Fowler's summary and conclusions follow: Organic gastric syphilis is more frequent than formerly supposed. The gross lesions of gastric syphilis are (1) gummas in various forms, and (2) diffuse infiltration. Specific ulcers result from the degeneration of gummas. Symptomatically such lesions differ from benign ulcers, chiefly in the absence of pain, ease from food and alkalies, less periodicity, anacidity, vomiting, with good appetite, excessive weight loss and improvement in gastric function with specific treatment. Without operation the diagnosis usually rests on the past history of early syphilis, present late syphilitic signs, Wassermann reactions and the therapeutic test. However, a negative Wassermann reaction does not exclude the possibility of gastric syphilis, and benign lesions of the stomach may occur in a known syphilitic patient. At operation specific ulcers are always multiple, ragged lesions occurring usually at the cardia, the lesser curvature, or the pyloric region accompanied often by perigastric adhesions, thickened gastric walls and gastric deformity. Large gummatous tumor masses or cicatricial contractions subsequent to extensive ulceration simulate carcinoma, particularly as regards the type of dyspepsia, the vomiting, the rapid loss in weight, and the anacidity, although the cachexia and loss of strength are less than that encountered in malignancy, and the course may have been longer. The operative findings consist usually of an irremovable gastric tumor mass indistinguishable from carcinoma. The roentgen-ray evidence also simulates carcinoma. The roentgenographic signs of gastric syphilis in general consist of encroachments on the lumen, distortions and deformities. The microscopic evidence consists of the characteristic syphilitic obliterative endarteritis and perithelial lymphocytic infiltration with atrophy of the mucous membrane and hypertrophy of the submucosa and muscularis. Postmortem confirmation of the diagnosis is infrequent.

Organic gastric syphilis may simulate (a) benign gastric ulcer, (b) gastric carcinoma, or (c) present an atypical gastric picture.

The diagnosis of organic gastric syphilis is often difficult and sometimes impossible.

A negative Wassermann reaction does not disprove the existence of syphilis, and a positive reaction does not prove that a gastric lesion is specific.

The therapeutic test is usually reliable but not infallible.

The roentgenographic evidence is not conclusive.

Exploration may not be determinative, particularly as regards differentiation from carcinoma.

Atypical, chronic gastric disorders, which are unresponsive to the usual treatment, should arouse suspicions of syphilis.

Fowler adds a case to his report of a gastric ulcer in a woman of 26, who did not respond to antisyphilitic treatment, although she was an undoubted syphilitic. Previous operations on this patient had given but temporary relief, and the pyloric half of the stomach, together with some large lymph nodes in the gastro-colic omentum, were removed. The pathologic examination showed a gastric ulcer with fibrous base, chronic inflammatory changes, and lymphadenitis in mild degree.

GOODMAN, New York.

THE CONSTITUENTS OF CHAULMOOGRA OIL EFFECTIVE IN LEPROSY. J. T. McDONALD and A. L. DEAN, J. A. M. A. **76**:1470 (May 28) 1921.

For fourteen and one-half months, a period ending the middle of March, 1921, the authors have been able to observe a series of patients with leprosy treated by their "standard treatment." This standard treatment consists of weekly intramuscular injections of the mixed ethyl esters of chaulmoogra oil carrying 2 per cent. of iodine in chemical combination. This is supplemented by the oral administration of the fatty acids and combined with 2.3 per cent. of iodine.

The following table shows the results of this treatment.

RESULTS OF TREATMENT

Number of patients, Jan. 1, 1920.....	72	
New patients received, Jan. 1, 1920 to March 15, 1921....	116	
Total number of cases.....		188
Deaths	7	
Paroled	94	
Total departures		101
Patients on hand, March 15, 1921.....		87

The authors' clinical observations appear to establish the fact that oral administration of chaulmoogra oil compounds are of doubtful value. Patients receiving injections alone did as well as those receiving combined treatment. They also believe that the therapeutic activity of chaulmoogra oil resides in the contained hydnocarpic and chaulmoogric acids. Patients treated with these acids in a pure state improved with the same rapidity as did those receiving the standard treatment. The authors state that "the fatty acids of the chaulmoogric series are specific in leprosy." Iodine appears to possess little therapeutic efficiency in leprosy.

Investigations at Kalihi Hospital have brought to light another substance in chaulmoogra oil which appears to possess the carbon ring characteristic of the chaulmoogric series, but is more highly unsaturated than either chaulmoogric or hydnocarpic acids. Clinical tests with this material indicate that it is particularly efficient therapeutically. However, investigation of it has not proceeded far enough to determine its true value.

MICHAEL, Houston, Texas.

USE OF PEPSIN IN DERMATOLOGY. F. P. CEPELKA, Ceska dermat. 2:92, 1921.

The use of a digestive mixture of pepsin and hydrochloric acid originated with Unna. His therapy is based on the fact that only the superficial layer of horny cells resists digestion, while the body of the cells consists of poorly digestible keratin B and easily digestible albumoses. In the cutis, the plasma and the connective tissues undergo digestion rapidly. Unna used his digestive mixture most successfully in the treatment of keloids, as they consist mostly of pathologically changed connective tissue. He also obtained good results in the treatment of hypertrophic scars from burns, lupus ulcers, acne indurata, lymphatic indurations and adenitis. The mixture controlled well exuberant granulations and cleaned and deodorized necrotic tissues. It makes a painless keratolytic for keratoma.

Unna's original formula is:

	Gm. or C.c.
R Pepsin	10
Hydrochloric acid	
Phenol	1
Distilled water	200

Later, for safety's sake, Unna reduced the amount of pepsin to 1 per cent. The digestive mixture is applied in the form of wet compresses, strictly limited to the treated area, and covered with impervious material. It is advisable to protect the surrounding skin by some bland ointment.

In view of the fact that during the process of digestion the cells become porous, and thus an osmosis takes place, it is possible to make use of this method to introduce into the skin, by means of osmosis, the substances to which the horny layer is otherwise impermeable, such as epinephrin, morphin, cocain, arsenic and other drugs.

Wassermann modifies Unna's technic. He advises the admixture of 10 per cent. pyrogallcollodium. Pepsin aids pyrogallol to penetrate, while collodium assures a localized application.

At the clinic in Prague the original Unna's technic is used with good and indifferent results. It was found most effective in the treatment of keloids and hypertrophic scars. Keloids flatten out, scars become more pliable, contractures stretch and give considerably. It is a long and drawn-out procedure in many cases, requiring a good deal of patience, but as it is often the only possible treatment at hand, it is worth trying. Care must be taken to stop short of irritation. The success depends to a large extent on careful application.

CEPELKA, Chicago.

DIAGNOSIS OF SYPHILIS AND GLAND PUNCTURE. H. DROOP, Dermat. Ztschr. 32:336, 1921.

The method of gland puncture for the diagnosis of early syphilis was first proposed by Hoffmann. The method is especially valuable in cases of inaccessible primary lesions, as when accompanied by phimosis, if the lesion has been treated, and if the demonstration of the spirochetes is complicated by types of organisms which simulate the *Spirochaeta pallida* and add confusion to bacterial diagnosis. Such organisms include the *S. refringens*, and certain so-called "intermediate forms" as *S. gracilis*, *pseudo-pallida*, *dentium*, etc.

Although spirochetes have been demonstrated in the glands in other conditions than syphilis, Castellani, for example, having found organisms similar to *S. pallida* in 50 per cent. of patients with frambesia, ordinary diseases in which the spirals have been said to exist, lung gangrene, lymphatic leukemia, Hodgkin's disease and lymphosarcoma add but little concern in differential diagnosis.

Droop examined the lesions of fifty patients with primary syphilis and of five with secondary cases. Of the primary cases *Spirochaeta pallida* was demonstrable in twenty-seven; an examination was not made in four; twice the examination was accepted as negative after one dark-field investigation; ten times the primary lesion could not be studied on account of accompanying phimosis. Seven times the examination was negative due to some local application.

Gland puncture in these fifty cases gave thirty-eight positive and twelve negative results. In the ten cases of phimosis, the spirochetes were demonstrated nine times: in five positive gland examinations, the concomitant lesion examination was negative. Droop notes that the positive diagnosis in fourteen cases of fifty depended on gland puncture.

GOODMAN, New York.

FURTHER CONTRIBUTION TO KNOWLEDGE OF RELATION OF ENDOCRINE GLANDS. JAROSLAV JEDLICKA, Ceska dermat. 2: Nos. 5-6.

(a) *A Case of Geroderma*.—The cases described in the literature under the names of geroderma, senilismus, senium praecox and progeria are not identical in details, each having its own peculiarities. They appear at different ages and from various causes, but clinically they all manifest themselves by premature old age with its senile degenerative cutaneous changes, premature grayness and loss of hair, and impaired sexual power. The disease is the outcome of a pluriglandular insufficiency with main changes in the thyroid and sexual glands. The author cites a case of a man of 36, aging beyond recognition within twenty months (apparently), without any other cause but war hardships. Besides senile appearance he showed lowered sexual power, general asthenia, paresthesias, tremor of extremities, a lowered nitrogen metabolism and increased carbohydrate tolerance. The patient improved remarkably under thyroid therapy.

(b) *Case of Myxedema Idiopathicum Adultorum*.—A woman suffering for twenty-one years from hypothyroidism showed all the typical consequences: The trophic changes in all ectodermal structures, a lowering of all vital processes and of general metabolism and physical changes. As a complication she had polyneuritis and anemia with lymphocytosis. The case illustrates besides the hypothyroidism a coexisting hyperpancreatism with high carbohydrate tolerance, and a lowered epinephrin glycosuric effect. It proves again that the thyroid stimulates the chromaffin system and antagonizes the action of the pancreas.

(c) *Exophthalmic Goiter and Diabetes*.—A middle-aged woman who had suffered with exophthalmic goiter for three years developed a severe case of diabetes and died. The case is cited as a contrast to the first two cases: Hyperthyroidism led to hypopaneatremism and an increased function of the suprarenals. Hypersuprarenalism increases the sugar concentration in the blood, and the coexisting hypopaneatremism still further interferes with the combustion of the sugar. The cause of glycosuria is, therefore, complicated.

CEPELKA, Chicago.

REGARDING DIFFUSE CONGENITAL HYPERKERATOSIS. J. GOLAY,
Ann. de dermat. et syph. **3**:97, 1921.

A girl, 3 weeks old, had been born with a brownish-yellow skin which markedly resembled a coat of collodion. It was fissured in places. The flexor surfaces were the more markedly involved; beyond ectropion of the lids there was no deformity. The sparse hairs of the scalp were unusually long. Minute sebaceous cysts appeared on the nose. Treatment with a bland ointment was instituted, but no relief was obtained, and the child died a month later with bronchial pneumonia. Necropsy revealed little of interest. A complete report is given, including the histologic examination of the skin.

The author considers congenital hyperkeratosis distinct from ichthyosis vulgaris, although at present they cannot be definitely distinguished histologically. The sites of predilection are exactly opposite. The congenital hyperkeratosis is present at birth, while ichthyosis vulgaris develops later, and is not congenital but hereditary. The former is usually incompatible with life; the latter is never. This congenital condition or malformation belongs probably in the same group as erythroderma ichthyosiforme and keratosis palmaris et plantaris.

The condition described may be due to tuberculosis in the mother, or to syphilis, or to a consanguineous marriage, but it is more probably toxic in origin. In the present case the child's mother had, during her pregnancy, consumed large quantities of salt to satisfy a craving. This she had also done during three of her six previous pregnancies, and all three had resulted in fetal hyperkeratoses and death at birth or soon after. The other children showed no trace of the condition. The author thinks that the salt may have had an ill effect on the kidneys, causing the circulation of toxic substances which influenced the fetal development. This is offered merely as a theory, to be tried in future work.

PARKHURST, New York.

TREATMENT OF PARESIS AND TABES. WAGNER-JAUREGG, Wien. klin.
Wchnschr. **34**:171, 1921.

As early as 1887, the author has noted that remission of paresis seemed to have been preceded by some acute febrile disease. He suggested that this phenomenon might be used therapeutically. A few years later (1890) he used Koch's tuberculin in conjunction with mercury and obtained very favorable results. More recently, he has used Besredka's typhoid vaccine to cause a febrile reaction, with equally good results. In 1917, he tried the injection of the parasites of tertian malaria. During the last two years he has used this method in a large series. He injects whole blood from a patient with malaria into the subcutaneous tissues of a paretic patient. After an incubation of from five to thirty-one days, typical chills and fever paroxysms occur. The temperature rises as high as 40 to 41 C. After eight or more paroxysms, the malaria is treated with intravenous injections of quinin, and simultaneously six injections of neo-arsphenamin at weekly intervals are given. With this treatment every patient with induced malaria has been cured. The results on the paretic symptoms have been better with this mode of therapy than with any other known to Wagner-Jauregg. He says it is interesting that the serologic and spinal fluid tests do not parallel the clinical course of the improvement.

The limitations to the method are that it can only be executed where there is endemic malaria, or else where the number of paretic patients is so great

that the plasmodium can be propagated among the paretics themselves. In this way the author has obtained about twenty-six successful passages of the malarial parasite.

GOODMAN, New York.

CASE OF EPIDERMOLYSIS BULLOSA. DR. SCHWANK, 2:30, 1920.

A man, aged 28, with a tuberculous and neuropathic family history, who was tuberculous and neuropathic himself, showed symptoms of vasomotor disturbances, dermatographism, acro-asphyxia, hyperhidrosis, and other conditions. According to the patient's story, his mother, one aunt, one sister and two brothers suffered from the same skin trouble he had, the main symptoms of which was weeping, recurring in the fall, lasting two to three months and disappearing spontaneously. The patient has had recurrences since he was 3 years old. The present attack was the most severe, localized, however, only on the left lower extremity. Vesicles first appeared in places bitten by a mosquito. New crops followed on the skin irritated by scratching and pressure of clothing. Vesicles came on without prodromal symptoms usually at night. Lesions healed without trace. It was possible to produce new vesicles experimentally by prolonged rubbing or pressure. Sudden trauma, no matter how intense, failed to produce them.

The author reviews the pathogenesis and etiology of epidermolysis bullosa. The patient in this case was tuberculous. His suprarenals also might have shown tuberculous changes with consequently altered secretion, possible irritation of capillaries, and increased lymph secretion. Weeping goes on indefinitely under an intensive irritation of vasodilations. The rapid response to treatment in this case would uphold the correctness of the theory. After the third injection of epinephrin (0.5 c.c. of 1:1,000) the weeping stopped completely. After five injections the lesions dried up and healed. Even the general condition improved, the patient losing his sensation of fatigue and depression. Once during the observation there was a marked improvement following a sexual excess. Cases of this type are probably the result of a combined disturbance of the glands of internal secretion.

CEPELKA, Chicago.

ANTISYPHILITIC THERAPY. A COMPARATIVE STUDY OF SOME INTENSIVE METHODS. LOUIS CHARGIN, J. A. M. A. 76:1154 (April 23) 1921.

Chargin studied the effect of three plans of intensive antisiphilitic therapy on 106 cases of early syphilis. These patients all presented early cutaneous manifestations of the disease and a strongly positive (+++ to +++) Wassermann reaction.

Thirty-seven were treated according to the method advocated by Pollitzer; that is, three full doses of arsphenamin were given on three successive days followed by six weekly injections of an insoluble mercurial salt. Nineteen patients received three or four injections of arsphenamin on alternate days, followed by six weekly injections of mercury, and this in turn by additional administrations of arsphenamin, three, four or five in number, a week apart or on alternate days. Fifty patients were given from six to eight injections of arsphenamin five days to a week apart, combined with ten to twelve injections of mercury at weekly intervals.

Wasserman tests were made at weekly intervals on all patients, and the results of the tests were used as a criterion of the efficacy of the method. So far as the clinical manifestations of the disease were concerned, each of these programs caused their disappearance with equal rapidity.

As a result of the study, it was found that the most intensive method had no advantage over the less intensive ones, and Chargin, therefore, concludes that the latter are to be preferred since they offer a greater margin of safety.

MICHAEL, Houston, Texas.

CONTRIBUTION TO THE DIFFERENTIATION OF GRANULOMATOUS SKIN DISEASES. L. ARZT, *Acta dermat.-ven.* **3-4**:365 (Dec.) 1920.

In April, 1913, a man, aged 25 years, appeared with an ulcer, 3 by 10 cm. in size, located in the right occipitonuchal region. It had started a year previously, heralded by an enlargement of the cervical lymph nodes, and had spread progressively in spite of local treatment, including the roentgen ray in semi-intensive doses. The ulcer had sharp, firm borders and a rough, purulent, necrotic base, reaching the bone. There were palpable lymph nodes in the neighborhood. The blood findings were normal, except an eosinophil count of 5 per cent.; the tuberculin reaction was negative; no tubercle bacilli or other apparently causative organisms could be found; syphilis was excluded by the therapeutic test; the favored guess was "mycosis fungoides d'emblée." With febrile exacerbations the ulcer extended, involving muscle and bone; there was considerable sloughing. The bacillus of glanders was sought in vain. There soon followed a lethal exitus. Necropsy revealed the presence of a granulomatous process with circumscribed nodules in the lymph nodes, liver and spleen. Here, as well as in a section from the ulcer, were found lymphocytes, plasma cells and large polygonal cells like those described by Paltauf and Sternberg. It was, therefore, a case of lymphogranulomatosis with *ulcus lymphogranulomatosum*. The primary involvement was probably in the lymph nodes rather than in the skin. This process stands near *mycosis fungoides*, especially the form *d'emblée*, in classification, but the necropsy and histologic examination easily show its distinguishing characteristics.

The discussion is interesting and the bibliography good.

PARKHURST, New York.

ETIOLOGY OF SARCOIDS OF BOECK-DARIER. B. REJSEK, *Ceska dermat.* **1**:113, 1920.

The majority of dermatologists believe that sarcoids or so-called tuberculids appear in persons suffering from manifest or latent tuberculosis. Tuberculids are caused either by the action of toxins (toxic theory), or by bacilli brought to the skin by the blood current or introduced into the skin from without (bacillary theory). Bacilli lodging in the skin are either usually dead or incapable of multiplication. Rarely they reach the skin alive, and in that case cause genuine tuberculosis of the skin with positive findings of the organisms in the sections.

The author believes that the blood of a patient suffering from latent or manifest tuberculosis always contains a certain number of toxins which may vary from time to time. If the variation takes place gradually the skin has time to adjust itself, while at the same time it becomes hypersensitive to all

other conditions. If the concentration of toxins increase suddenly, a reaction takes place with the formation of some form of tuberculid without the direct action of the tubercle bacillus. Different types of tuberculids can appear at the same time. The number of lesions depends on the number of toxins produced above the tolerated concentration. The author's case illustrates the simultaneous appearance of lichen scrofulosorum on the face and miliary lupoids of Boeck-Darier on the body in a woman with active pulmonary tuberculosis. The article contains a detailed description of lesions with histologic findings.

CEPELKA, Chicago.

ICTERUS SUPERVENING TWO MONTHS AFTER ARSENICO-MERCURIAL TREATMENT IN A CASE OF SECONDARY SYPHILIS. RESUMPTION OF ARSENICO-MERCURIAL TREATMENT. GRAVE ICTERUS. LETHAL EXITUS. P. RAVAUT, *Bull. soc. franç. de dermat. et syph.* **2**:57, 1921.

A girl, aged 18, had a genital chancre and a secondary eruption. She was first given mercuric cyanid (1 c.c. of a 1:100 solution, intravenously) daily for five days. Then weekly injections of neo-arsphenamin were begun and she received eight of them in doses increasing from 0.2 gm. to 0.75 gm. with fourteen injections of the cyanid interspersed. A slight urticaria followed the first injection of neo-arsphenamin. At the end of this course an acute anginal infection occurred; during convalescence eight injections of strychnin cacylate were administered; icterus appeared with chills, nausea and vomiting. The administration of calomel brought no relief, small doses being employed. The liver was large and tender, and there was some splenic enlargement. Antisymphilitic treatment was resumed, with seven injections of mercuric cyanid (as above) and two of neo-arsphenamin (0.1 and 0.2 gm.). There was an exacerbation, two more small doses of neo-arsphenamin were given, and the patient soon died in coma. No spirochetes could be found in the liver, and it was concluded that there had been a toxic hepatitis, possibly due to arsenic.

PARKHURST, New York.

EFFECT OF INTRAVENOUS ADMINISTRATION OF ARSPHENAMIN, NEO-ARSPHENAMIN AND MERCURY. ROBERT A. KILDUFFE, *J. A. M. A.* **76**:1489 (May 28) 1921.

This investigation was actuated by the recent report of Strickler, Munson and Sidlick on the effect of arsphenamin on the Wassermann test in non-symphilitic patients. It will be remembered that these workers reported the production of positive complement fixation following the intravenous injection of arsphenamin.

Kilduffe used rabbits whose serum was consistently Wassermann negative. To one set of animals he gave three intravenous injections of arsphenamin solutions in doses of 0.01 gm. per kilogram of weight, equivalent to 0.6 gm. per 60 kg., or the weight of a young adult. The second series received three intravenous injections of neo-arsphenamin solution in doses of 0.02 gm. per kilogram of weight, equivalent to 1.2 gm. per 60 kg. A third series received intravenous injections of solutions of mercuric chlorid in doses of 0.00033 gm. per kilogram of weight, equivalent to 0.0193 gm. per 60 kg.

The drugs were given at weekly intervals and blood for Wassermann tests was taken just prior to each injection.

The results were uniformly negative, a positive Wassermann reaction not being produced in any animal of any series. Kilduffe believes that these findings are significant and indicate the necessity for further investigations of this subject.

MICHAEL, Houston, Texas.

WHAT ARE PARTS PLAYED BY MERCURY AND BACTERIA RESPECTIVELY IN PATHOGENESIS OF MERCURIAL ULCERATIVE STOMATITIS AND COLITIS? J. ALMKVIST, *Acta dermat.-ven.* **3-4**:312 (Dec.) 1920.

In an exhaustive article with an extensive bibliography, the author thoroughly considers this question, and arrives at these conclusions:

1. The bacteria acting in mercurial ulcerative stomatitis and colitis are not specific bacteria, but albumin-decomposers of various kinds.

2. These bacteria play their rôle in a two-fold manner: First, by the process of decomposition, they give rise to local erosions of the mucous membrane and a local formation of hydrogen sulphid which, together with the mercury in the tissue, produces local tissue necroses. Second, they convert the tissue necroses that have arisen into putrid progressive ulcerations.

3. The rôle of the mercury is this: In combination with the locally absorbed hydrogen sulphid gas, it causes intercellular mercury sulphid deposits in the endothelial cells of the capillaries which, by damaging these cells, check the formation of the tissue fluid, thereby provoking local tissue necroses. These tissue necroses improve the substratum for the bacteria which multiply in it enormously, their virulence being thus increased so that they are able to attack healthy tissue. The final outcome of mercurial action is, in other words, a powerful furtherance of the development of the albumin-decomposing bacteria.

PARKHURST, New York.

CONSIDERATIONS REGARDING CLINICAL VALUE OF BORDET-WASSERMANN REACTION. C. ABADIE, *Bull. Soc. franç. de dermat. et syph.* **2**:54, 1921.

The results of the Wassermann test do not coincide with our present conception of the laws of immunity; we have only a vague idea of its significance. It is therefore urged that we interpret its results only in the light of all the clinical findings assembled. Undue reliance must not be placed on it, in diagnosis and especially in treatment.

PARKHURST, New York.

NEW CONCEPTIONS RELATIVE TO THE TREATMENT OF MALIGNANT DISEASE, WITH SPECIAL REFERENCE TO RADIUM IN NEEDLES. W. L. CLARK, *Pennsylvania M. J.* **24**:214 (Jan.) 1921.

Clark states that the use of radium needles has revolutionized radium technic. Results are obtained by this method that cannot be secured by the application of radium in plaque or capsule. The needles are particularly efficacious in the treatment of growths too large for radium penetration from the outside by capsule or plaque. With the newer method malignant growths situated in the intestines, omentum, larynx, frontal sinns and other locations difficult of access, are not entirely hopeless.

Clark uses needles made of "noncorrosive steel," of various length and style of point, all having a wall thickness of 0.3 mm. Each contains from 5 to 10 mg. of a radium salt.

No definite rules of technic can be given since every case is a law unto itself. Generally speaking, needles are placed in sarcomatous tissue 20 mm. apart and withdrawn in twelve hours. In carcinomas, the needles are placed 25 mm. apart and removed in from eighteen to twenty-four hours.

The use of radium needles is only in its infancy; yet even without definite knowledge as to technic, a great deal has been accomplished. The future will show this method to be of even greater potency.

MICHAEL, Houston, Texas.

HYPERKERATOSIS EXCENTRICA. J. BUKOVSKY, *Ceska dermat.* **2**:61, 1920.

The author reports a case of hyperkeratosis excentrica that showed all the typical symptoms of the condition as described by Mibelli under the term of porokeratosis. The article contains a histologic study of the skin findings, especially the early changes. The author arrives at the following conclusions: From an unknown cause, areas of porokeratosis appear early in life in different localities. These centers of porokeratosis become more numerous with each attack. Each center first appears as a tubercle enlarging peripherally. After a varying length of time, the oldest part of the condition begins to desquamate and the lesions assume a new form—a deepened scaling center with a porokeratotic, hard border without desquamation. If the scaling reaches the periphery, the entire lesion flattens out and becomes barely noticeable; a recurrence may, however, take place. The course of the disease may last for years; even changes in individual lesions take place slowly. The treatment is ineffective, ameliorations being only temporary.

The author believes that the term "porokeratosis" is ill-fitting, and prefers Respighi's name "hyperkeratosis excentrica" or Respighi and Dyerea's term "hyperkeratosis figurata centrifuga atrophicans."

CEPELKA, Chicago.

SOME EXPERIMENTS ON THE VOLATILIZATION AND ABSORPTION OF MERCURY. C. E. JENKINS, *Brit. J. Dermat. & Syph.* **33**: 135 (April) 1921.

Jenkins conducted experiments on the volatilization of mercury at blood heat, placing the metal in incubators kept at that temperature, and found no volatilization of the metal.

A second set of clinical experiments was conducted, four patients being given mercury inunctions under conditions which allowed little opportunity for inhalation of any of the metal which might have been volatilized, and the author feels that the onset of mercurialism was as rapid as one could expect after inunction in the usual way.

He therefore concludes that the rate of volatilization of mercury at blood heat is insignificant, and that in the inunction method of administering mercury the metal is absorbed through the skin.

SENEAR, Chicago.

CASE OF SYPHILITIC REINFECTION. H. BREIDE, *Acta dermat.-ven.* **3-4**:456 (Dec.) 1920.

A man, aged 25 years, was seen July 25, 1917, with a chancre in which the spirochetes of syphilis were found. He received ordinary mixed treatment, with neo-arsphenamin and mercurial injections for four courses.

June 24, 1920, he and a comrade were exposed with the same woman, and three or four weeks later a genital ulcer appeared, not in the location of the lesion of 1917. There were the typical satellite lymph nodes in the groin, and *Spirochaeta pallida* was found in the ulcer. The Wassermann reaction was negative, and continued so during treatment, which was energetic.

(In this same issue, under the heading, "Clinical Reports," Almqvist publishes two cases of syphilitic reinfection. Both occurred in men who transmitted their first infection to their consorts, were apparently cured, and then presented new initial lesions, having had no extra-marital intercourse in the interim.)

PARKHURST, New York.

IODIN IN CEREBROSPINAL FLUID, WITH SPECIAL REFERENCE TO IODID THERAPY. E. D. OSBORNE, J. A. M. A. **76**:1384 (May 21) 1921.

Kendall's method was employed in this investigation. Iodin was found in normal cerebrospinal fluid in an average amount of 0.018 mg. per 100 c.c. None of the patients on whom this determination was made had received any therapy by mouth for the previous three or four months.

Increased amounts of iodine were present in the cerebrospinal fluid after the administration of potassium iodid by mouth and rectum and following the injection of sodium iodid intravenously. After the latter method of introducing the drug, a definite curve of the iodine content of the cerebrospinal fluid can be plotted. This curve depends on the amount administered.

In four neurosyphilitic patients who were receiving sodium iodid intravenously, large amounts of iodine were found in the cerebrospinal fluid. The fluid from one patient contained 42.308 mg. per 100 c.c., while the others approximated 4.5 mg. for the same amount of fluid.

These four observations point to one or both of two possibilities: either the meninges are more permeable to iodine compounds when there is meningitis or tissue actively involved by syphilis takes up more iodine than normal tissue.

MICHAEL, Houston Texas.

RECURRENT PHLYCTENULAR ERUPTION ON EXTREMITIES WITH MENINGEAL REACTION. L. CHATELLIER, Ann. de dermat. et syph. **3**:151, 1921.

In 1914, a man of 21 years, first noticed on his hands an outbreak of vesicles which lasted several weeks, accompanied by a tingling sensation. The attacks continued at intervals of a few weeks. According to the history, the grandmother and an aunt had previously suffered from similar trouble.

The lesions were found to be vesiculopustular, involving the nails as well as both surfaces of the hands. There was no itching. Redness and desquamation were features. The blood showed a small mononuclear leukocytosis, and the spinal fluid, though otherwise apparently normal, showed 24 lymphocytes per cubic centimeter. The lesions correspond to those of Hallopeau's "acrodermatite discontinue." There is given a brief review of similar cases in the French literature. The possibility of a relationship to erythema multiforme is considered, although the lesions here were essentially monomorphous and the subjective symptoms were slight; neither was there an eosinophilia. The meningeal reaction is remarkable.

PARKHURST, New York.

EOSINOPHILIA AND ITS RELATION TO SKIN DISEASES. V. SVESTKA, Ceska dermat. 1:73 and 96, 1920.

The first part of the paper discusses the phenomenon of eosinophilia in general, its relation to infections and anaphylaxis. It reviews the theories about the origin of eosinophils from the bone marrow and possible transformation of neutrophils into eosinophils. The author believes in the possibility of extramedullary origin of eosinophils and in local histogenesis of eosinophilic cells in the skin and mucous membranes.

Svestka studied ten cases of scabies in regard to blood changes, and tabulated his results. Untreated patients show a high degree of eosinophilia (31.05 per cent. in Case 1). The number of eosinophilia cells decreased rapidly under treatment. Eosinophilia results from the irritation of the organism by toxic products of the vital activity of parasites, and will increase in proportion to their activity; it is independent of skin findings.

A high degree of eosinophilia was found in dermatitis herpetiformis (58 per cent.). At a certain stage of development the bullous lesions show eosinophil cells only; later neutrophilic leukocytes and lymphocytes also make their appearance. There is a direct relation between the temperature and blood eosinophilia, which is the highest at the height of fever.

CEPELKA, Chicago.

CURE OF MELANOTIC TUMOR AND MELANOTIC SPOTS BY MEANS OF RADIUM THERAPY. S. MENDES DA COSTA and J. PAPE-GAAY, Acta dermat.-ven. 3-4:309 (Dec.) 1920.

A woman, aged 84 years, had a tumor near the inner canthus of the eyelid and a spot, diagnosed lentigo senilis, on the nose. For fear of metastasis a biopsy was not made. A round, flat metallic plaque, 1.5 cm. square, containing 2.5 mg. of radium sulphate, was applied with a tin filter, 0.2 mm. thick, for six hours at a time, every two days for two weeks, then weekly for three treatments with 0.1 mm. of tin. Three months later two small black spots remained, which were treated twice for three hours through 0.05 mm. of tin and once for six hours through 0.1 mm., at intervals of one week. Not a trace remained, and there has been no recurrence in two years.

A girl of 20 years presented two black spots about the nose, of six and three years' duration, one appearing papular. Radium bromid, amounting to 10 mg., was applied with good results.

PARKHURST, New York.

INFLUENCE OF METEOROLOGIC CHANGES ON SKIN DISEASES. KAREL HUBSCHMANN, Ceska dermat. 2:19, 1920.

Dr. Bettmann published in the *Münchener medizinische Wochenschrift*, 1920, No. 23, an article dealing with the unquestionable influence of meteorologic changes in the spring on the human organism, especially the increase in the growth of hair and nails, and increase in the secretory activity of sweat and sebaceous glands, depending probably on the increased activity of the glands of internal secretion.

Two cases of dermatitis exfoliativa generalisata observed at the hospital of Prague are described in a preliminary report of the author. They further illustrate Dr. Bettmann's observations, and show the changes in a dermatosis under varying atmospheric conditions. The first patient, a woman of 50, showed a definite undeniable aggravation in the skin condition, with a mental

depression from six to twelve hours before a sudden fall of atmospheric pressure. As she showed signs of hypothyroidism, she was put on thyroid therapy with wonderful success. Her condition cleared up completely. It is difficult to state whether, or to what extent, spring influenced this syndrome.

CEPELKA, Chicago.

CASE OF GLANDERS IN MAN. CLEMENT, Bull. Soc. franç. de dermat. et syph. **2**:63, 1921.

A member of the Corsican hussars contracted the disease from horses in his regiment. Signs of a general infection first appeared: fever, epigastric pain, vomiting, headache and general malaise. That which dominated the scene was a syndrome of suprarenal insufficiency, with marked hypotension. Some time later abscesses appeared successively on the left calf, the dorsum of the hand and the forehead. The first was evacuated, and the others were cauterized by heat. The bacilli were found in cultures. A few days later the face became greatly swollen, and there were fetid ulcerations of the cheek and hand. The patient became rapidly comatose and died, more than three months after the onset of the infection. A vaccine was prepared too late to be of service.

PARKHURST, New York.

A CASE OF ORIENTAL SORE (OF ITALIAN ORIGIN) ENCOUNTERED IN THE UNITED STATES. R. D. SPENCER, J. A. M. A. **76**: 1494 (May 28) 1921.

An Italian, aged 18, a recent immigrant into this country, had a large sore on his right cheek and two smaller but similar lesions on his left wrist. The lesions had all appeared while the patient was still living in Italy.

The sore on the face was 3 cm. in diameter; its margin was brownish red, slightly wavy and elevated, merging and fading into the surrounding normal skin, indurated and not painful on pressure. The base of the lesion was covered by a brownish crust, which when removed revealed a raw, red, granular bleeding surface.

Smears from the lesion showed numerous typical leishmanias. Cultivation was unsuccessful. Inoculations into a rabbit, a guinea-pig and a snake were without result.

Treatment with carbon dioxid snow was followed by prompt cure.

MICHAEL, Houston, Texas.

MULTIPLE CHANCROIDS IN CASE OF SCABIES. JAROSLAV POHL, Ceska dermat. **2**:77, 1920.

The patient was treated in the hospital for scabies. The second or third day after taking a bath in a tub previously used by the patients from the venereal ward, he noticed a small ulcer on the penis, soon two more in the same locality, and several others on the thigh. They developed into chancroids. The secretions and sections from the ulcers contained Ducrey-Unna's streptobacilli. The case illustrates the possibility of extragenital localization of chancroids in the course of other generalized dermatoses, especially scabies, with its many lesions of the epidermis. It is a well-known fact that a scabetic skin is susceptible to pyogenic infections and extensive impetiginous processes.

The macroscopic appearance in the given case might lead to difficulty in diagnosis. The chancroids do not respond to treatment as rapidly as a more superficial impetigo.

The patient's story (infected in the bath-tub) might have been truthful. *Streptobacillus*, just like the gonococcus and *Spirochaeta pallida*, can keep its vitality for a certain length of time in a moist medium. The case teaches the importance of the observation of strict hygienic precautions in venereal wards.

CEPELKA, Chicago.

SACHS-GEORGI REACTION AS A SUBSTITUTE FOR WASSERMANN REACTION. J. A. MURTO, *Acta dermat.-ven.* **3-4**:446 (Dec.) 1920.

In a series of 1,000 serums the author found that the two reactions agreed in 92.6 per cent. of cases. The new method seems especially valuable in diagnosing latent cases. The preparation and dilution of the extract is considered, this being the nucleus of the reaction. It is of course advantageous that the serum be fresh, although the author has obtained good results with serums four or five days old, and even six.

The reaction of Sachs-Georgi is much simpler of execution than the Wassermann test, and it seems as accurate and useful; it is also less expensive as regards materials. It is hoped that it may soon be substituted for the other, more arduous method.

PARKHURST, New York.

ON CREEPING DISEASE. HARUKICHI TAMURA, *Brit. J. Dermat.* **33**:138 (April) 1921.

The second part of Tamura's article considers first the clinical character of the line produced by the larva, and he describes erythematous, papular and vesicular types. He then discusses the histologic changes which have been found in the nine cases, including his own, studied from this standpoint. He again states that, while the *Gastrophilus* larva has been accepted as the cause of the disease, the *Gnathostoma* and *Hypoderma bovis* have now been found to be causative in some cases, and he predicts that other parasites will be incriminated in the future.

SENEAR, Chicago.

TWO CASES OF TABES WITH GASTRIC CRISES, TREATED BY NEO-ARSPHENAMIN. LEREDDE, *Bull. Soc. franç. de dermat. et syph.* **2**:47, 1921.

The first man, 35 years of age, was given 22.6 gm. of neo-arsphenamin during thirteen months, and the second, aged 48, received a total of 45.15 gm. in thirty-three months. In both cases the gastric crises were persistent at first and seemed to be aggravated by the treatment, but as the injections were continued the attacks became less and less frequent and finally disappeared entirely. Leredde emphasizes that treatment must be continued in spite of a pseudo-aggravation of symptoms. Even the mildest case, he says, must receive the most vigorous treatment, for the apparently mild cases are often harder to influence than the more severe. The treatment by daily injections (Sicard) is discouraged as productive of too much pain in these cases.

PARKHURST, New York.

PITYRIASIS RUBRA PILARIS. V. SVESTKA, Ceska dermat. **1**:126, 1920.

The author considers pityriasis rubra pilaris as a definite dermatologic entity and not a disease of the lichen group. His case, in a woman of 40, with otherwise negative findings, shows a well established clinical picture.

The author considers a disturbance of internal secretions as the possible etiologic factor. The article is illustrated by three photomicrographs of sections from involved skin.

CEPELKA, Chicago.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SYPHILITIC MASTITIS. R. BURNIER, Paris méd. **11**:292, 1921.

R. Burnier quotes from the records thirty-one cases and adds two to the list in which mastitis of syphilitic origin developed during the secondary or tertiary phase of syphilis; in three cases the syphilis was inherited. Trauma was not incriminated in any instance. The swelling of the gland may occur with or without pain, and it often simulates cancer. The lesions generally subside in a few weeks whatever treatment is used, but in four of the cases several months elapsed before the conditions returned to normal. The assumption of a syphilitic origin should not be rejected too hastily. Only twenty of the total cases were in women, but there was no connection with a pregnancy except in one case.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, April 5, 1921

HOWARD FOX, M.D., *Chairman*

CHRONIC CIRCUMSCRIBED PAPULAR NEURODERMATITIS, INVOLVING THE AXILLAE, BREASTS AND PUBIC REGIONS. Presented by DR. CLARK.

Miss H. Von L., 19 years of age, born in the United States, a stenographer, had a negative family history and her health was good. The trouble for which she was presented began eighteen months previously, when the patient first noticed severe itching in both axillae, which was soon followed by small firm, dry, conical, flesh-colored or pinkish papules that were intensely itchy. The number of papules slowly increased, with extension toward the trunk beyond the hairline. The papules were distinctly grouped, but showed no tendency to coalesce. Later, there was a distinct loss of hair, and the remaining hairs seemed dry, some of them being broken and stubbed. Two months ago, similar lesions appeared in a circular arrangement along the areola around both breasts, in a single row, and at the same time similar lesions developed along the upper margin of the hairs in the pubic region and the margins of the labia majora, and papules with macerated tops also appeared on the fourchette and inner surfaces of the labia majora. In the axillary region, the skin involved showed a succulent infiltration and thickening, with an exaggeration of the normal skin folds. None of the lesions had disappeared, and the itching had become intense, even excruciating.

The chemical analysis of the food showed that it was normal; blood sugar, 90 mg. per 100 c.c.; urea, 5.1 mg. per 100 c.c.; uric acid, 1.07; creatinin, 1.01.

A biopsy showed a moderate acanthosis with lengthening of the epidermal pegs and a round-cell infiltration in the derma around dilated capillaries, together with some edema of the cells of the papillary processes of the derma. The deep sweat glands looked cystic, some containing granular material. There was a moderate round-cell infiltration around the hair follicles. As the groups of dilated sweat ascini seemed to lie beneath the hair follicles and the occluded ducts, this dilatation may have been due to involvement in an inflammatory process about the follicles.

DR. CLARK said that the case agreed in every particular with the two cases reported by Dr. George Henry Fox, with the exception that the lesions involved also the pubic region, the labia majora and the breasts. The itching was a serious feature of the case, and he asked for suggestions as to treatment.

DISCUSSION

DR. LANE agreed with the diagnosis, but said that it was rather unusual to have the condition so closely confined to the hairy region of the axilla. It

usually spread a little forward. He then asked whether roentgen-ray treatment had been employed, and, on being answered in the negative, said that that seemed to be the most promising treatment.

DR. HOWARD FOX said that the case corresponded closely with the ones his father had originally described and with a few that he had observed. He had that same day seen the eruption in a young woman who stated that her mother suffered from a similar condition. Both mother and daughter had had the disease since birth, but, unlike other patients with this disease, had never complained of itching. In another patient whom he had shown at a recent meeting, rapid improvement was being obtained with the use of roentgen rays.

CASE FOR DIAGNOSIS. Presented by DR. CLARK.

H. P., 38 years of age, born in Greece, was a clerk. His family history was negative and his general health had always been good. He had had syphilis in 1904, with a mild secondary eruption. For the past five or six years his fingers had been sensitive to cold and inclined to get purple during the winter months. Three months ago the middle finger of the left hand rather suddenly became violaceous in color, slightly swollen and somewhat numb. This condition had persisted, without much change except for a short period about a week ago, when the finger became swollen following an injury.

On examination, the whole finger was of a violaceous color, terminating in a sharply irregularly-shaped border at its base. The affected region presented a rather dry and shiny appearance, and in certain lights there appeared to be lichenification throughout the lesion. There was no infiltration of the skin, but the finger gave the impression of being slightly enlarged, and it was held stiff and straight. The fingernail was slightly chipped off, as were some of the other nails. There was a distinct tremor of the hand, and while the finger could be flexed naturally, there seemed to be some loss of muscle power in it, as well as a pronounced loss of power in the thumb and muscular atrophy between the thumb and first finger of that hand. The patient showed no distinct nerve disturbance other than a mild exaggeration of the deep reflexes and a diminution of superficial reflexes in various parts of the body.

The Wassermann reaction was negative, and radiographs of the finger showed no abnormality of the bony structure. The patient exhibited a few irregular and circular furfuraceous, scaly lesions on the upper area that looked like tinea versicolor. There had never been any pain or itching in any of the lesions.

DISCUSSION

DR. LANE inquired whether the patient had ever had any chronic paronychia, and on being answered in the negative said he had no diagnosis to offer.

DR. ABRAMOWITZ thought the possibility of a factitious eruption should be considered. The lesion did not conform to any other type of skin disease.

DR. CHARGIN inquired whether lupus erythematosus had been considered. There was some scaling suggesting that condition, and that possibility should be ruled out.

DR. LEVIN said that clinically the patient presented an acrocyanosis of the finger, and there was no scaling. He considered this condition a result of the application of a chemical, or some constriction at the base of the finger.

DR. WISE said that the patient presented also scaly and circinate lesions on the right arm at its inner aspect, which were probably ringworm. The possibility of dermatophytic infection of the hand should therefore be considered.

DR. GILMOUR remarked that he had noted a light erythematous lesion on the back of the hand which suggested the possibility of lupus erythematosus appearing later.

DR. KINGSBURY, referring to an inquiry that had been made about the fingernails, said that the man gave a history of trauma—the fingernail having been caught in a door—and stated that he had used numerous applications. The appearance suggested a phenol burn, and that possibility should be considered.

DR. CLARK added that the injury was sustained some time after the appearance of the lesion, and applications were made; after the inflammation subsided the appearance was about the same as before the injury.

DR. HOWARD FOX said that the appearance of the finger suggested erysipeloid—a condition that was often due to handling crabs. This, however, was ruled out by the history and course of the disease. He was unable to make a diagnosis of the case.

DR. CLARK said he would have a biopsy made and would report on it later.

ATROPHIC FOLLICULITIS. Presented by DR. LEVIN.

L. W., a married woman, aged 29, stated that she had had the black spots on the skin for two years. Scattered over the face, neck, trunk and extremities, there was a generalized condition of the skin characterized by the presence of pinpoint to pinhead sized and slightly larger black spots. These were not elevated but were level with the surface of the skin or were slightly depressed, and were situated in the mouths of the pilosebaceous follicles. These plugs could not be expressed, but after persisting for a variable period of time would fall out, leaving atrophic spots. The whole cutaneous surface except the palms was studded with the discrete black spots and atrophic lesions.

DISCUSSION

DR. WISE said he had seen the patient when presented at another meeting. At that time, no definite diagnosis was made, but one of the speakers had suggested acne keratosa of Croker. That, however, was not accepted. The picture presented by the patient was unique in the experience of the speaker, and he was not aware of having read a description of a condition to fit the case.

DR. LEVIN said that he had not known that the case had been presented before. He did not consider the condition to be acne, for there were no papules or pustules. He preferred calling it an atrophic folliculitis because it consisted essentially of a hyperkeratosis of the pilosebaceous follicles, with the subsequent dropping out of the plugs, leaving the lesions from pressure atrophy.

ERYTHEMA INDURATUM. Presented by DR. OCHS.

R. L., a girl, aged 17, a stenographer, when first seen, early in February, presented a number of nodules in the skin of the outer aspect of the right leg. The arrangement of the nodules was more or less serpiginous in outline. Soon, however, they formed a nearly complete ring. The nodules were bluish red in color, were hard and painful to the touch and ulcerated; they would heal and ulcerate again. When the patient was first seen, the lesions resembled a serpiginous syphiloderma. The Wassermann test, however, was negative. In

spite of the negative Wassermann reaction, the patient received eight intravenous arsphenamin injections. Two or more Wassermann tests proved negative, and the lesions were not influenced by the treatment. A few days before presentation a new nodule appeared, somewhat larger than the old lesions, red, indurated and tender to the touch. This lesion was fairly typical of erythema induratum.

DR. OCHS supplemented the history by stating that the patient was the oldest child of eleven pregnancies, of which there were only three children living. The mother had had eight miscarriages, the terms being from four weeks to four months. The girl was apparently well until she was 15 years of age, when after a fall she had a little abrasion which ulcerated, and a few weeks later a series of small bumps or nodules appeared, shaped somewhat like a horseshoe. At first he had thought that the lesion was a syphilid.

DISCUSSION

DR. WISE said it was a difficult case to diagnose. He did not think it was syphilis. It might be the superficial sarcoid of Boeck, probably a benign miliary lupoid. It was not erythema induratum, for there was not enough infiltration in the depths of the tissue.

DR. LEVIN asked whether there had been any ulceration, and on receiving a reply in the affirmative, said that the fact that ulceration did not occur in the multiple benign sarcoid of Boeck would indicate that the case was not that type of sarcoid. He favored the diagnosis of erythema induratum.

DR. HOWARD FOX said that at first glance the eruption appeared to be a nodular syphilid. As this was excluded by the therapeutic test, he suggested the possibility of a sysosis, as there was a marked hypertrichosis of the leg.

KERATOMA SYPHILITICUM. Presented by DR. WISE.

F. T., 52 years of age, an American, single, a housekeeper, presented herself at the Vanderbilt clinic with a skin eruption on the plantar surface of both feet, which had been present for fifteen years. She admitted having had an initial lesion, followed by a secondary eruption twenty years ago. At that time the only form of treatment taken by the patient was pills, which had been taken for six months. When recently seen, she presented a verrucous mass interspersed with deep fissures, confined to the plantar aspect of both heels—the condition of the right was more serious than that of the left. The right heel had been involved for fifteen years and the left heel for two years. The Wassermann reaction was + + + +.

DISCUSSION

DR. LANE said he had seen the patient two weeks before, and the condition had improved very much since that time.

DR. HOWARD FOX said that he, too, had seen the patient two weeks previously, and there appeared to be some improvement following the antisyphilitic treatment. The fact that the eruption was bilateral was, however, not in favor of a late syphilis.

LUPUS VULGARIS SIMULATING LUPUS ERYTHEMATOSUS. Presented by DR. LEVIN.

S. P., a man, aged 34, a native of Austria, had arrived in this country seven weeks prior to presentation. He stated that he had had the condition of the

skin for six months. On the left cheek there was an irregularly round patch the size of a half dollar. The center of the lesion was depressed and atrophic. The border was elevated and made up of pinhead-sized apple-jelly tubercles, which were very soft, as shown by compression with a toothpick. Scattered over the lesion were several characteristic tubercles. In the lower portion was an area which was white and scaly as the result of a trichloracetic acid application. On the right cheek was a smaller patch which was flat and scaly from acid applications.

DISCUSSION

DR. LANE agreed with the diagnosis.

DR. LEVIN said he had placed a question mark after the duration of the disease because he had discovered that the patient had received treatment abroad for years.

NEVUS UNIUS LATERIS. Presented by DR. LEVIN.

W. B., a schoolboy, aged 13, had had the condition of the skin since he was 5 months old. A small patch on the back of his neck had grown gradually and was followed by other patches on the neck, scalp and forehead. The skin on the middle of the forehead was covered by a linear elevated lesion with a verrucous surface covered with dirty grayish scales. The tip of the left ear was covered by a patch with similar characteristics. The left half of the neck showed similar linear lesions, extending from the scalp to the clavicle and forming rectangular and triangular figures with enclosed areas of normal skin. On the occipital region of the scalp was a flat, bald, white patch. Treatment had consisted of exposures to filtered and unfiltered roentgen rays, with good results—all the lesions were much flatter than when first seen, and the flat patch on the scalp had been the most elevated and warty.

DISCUSSION

DR. ROSTENBERG doubted the permanent effect of the roentgen rays and suggested that the lesions could be destroyed by fulguration. He then cited a case in which the same type of lesion was found, the size of a silver dollar, which was fulgurated four times and disappeared without leaving a scar. He was inclined to think that this method would be better in this case than the use of the roentgen rays.

DR. WISE said that it had been the experience at the Vanderbilt clinic that the result of roentgen-ray treatment was only a temporary disappearance of the keratosis, and that when the treatment ceased the keratosis was likely to disappear. He agreed with Dr. Rostenberg that the best treatment was either fulguration, the use of the actual cautery, or the curet.

CASE FOR DIAGNOSIS. Presented by DR. SCHEER.

G. B., a girl, aged 7 years, had been brought to Dr. Fordyce's clinic about ten days prior to presentation. At birth, the child's mother noticed a roughness of the lips, which gradually increased and was well marked when the patient was 1 year old. The mother also stated that the lesions varied in size—at times being very prominent, at other times barely noticeable. The lesions were limited to the mucous surface of the lips and adjoining buccal mucosa, and consisted of closely set nodules whose average diameter was one eighth of an inch; they were elevated from about one tenth to one eighth of an inch above the

surface of the lips. The color was that of normal mucous membrane, but when the lips were stretched the nodules appeared through the mucous membrane as yellowish-white bodies of firm consistence. On puncture no fluid contents could be obtained. There were no subjective symptoms. A biopsy was not permitted. The probable diagnosis was nevus.

Dr. Scheer said that he would like to have some suggestions as to treatment.

DISCUSSION

Dr. LANE suggested the diagnosis of lymphangioma.

Dr. WISE did not see any indications of angioma about the lesion. It might possibly be a lymphomatous nevus. The child showed a remarkable distortion of the teeth, and whether the same embryonic factor that caused the trouble with the teeth might not also have something to do with the lesions on the lip should be considered—for it undoubtedly appeared to be some form of nevus. When the lesions were palpated between the fingers they did not give the impression of a drop of water in the mucosa, but seemed rather more like sebaceous cysts.

NEUROTIC EXCORIATIONS. Presented by Dr. BECHET.

E. S., aged 47, from Dr. Trimble's service, stated that he had smoked opium extensively for eight years. For the past twelve or fifteen years this had been discontinued and morphia substituted. The latter drug was injected in the arms, an average of 60 grains a week being used. Seven months previously, while walking in the country, he was bitten very severely by "red bugs." Since that time, for no apparent reason, he had been in the habit of pinching the skin between the nails in order to get what he called "water" out. He stated that he frequently had to use all the strength in his fingers in order to expel this water. His wife had scabies and a positive Wassermann reaction. His Wassermann reaction was negative, and his disease antedated that of his wife. He presented for examination a considerable number of excoriated lesions, irregularly distributed in accessible parts of the body. The older lesions were pigmented; a few of the newer ones presented a bruised-like appearance.

DISCUSSION

Dr. SCHEER said that the itching might have been caused by morphin. Morphin habitués frequently suffered from obstinate pruritus.

Dr. BECHET replied that the man did not complain of itching, but passed hours of his time in picking and pinching the skin. The patient was plainly neurotic, and in his estimation presented a typical picture of "picker's disease."

CASE FOR DIAGNOSIS. Presented by Dr. WISE.

A. S., 48 years of age, white, born in Russia, but living in the United States for five years, was a shoemaker by occupation. He presented himself at the Vanderbilt clinic with a generalized eruption of two years' duration. The face presented a dusky reddish-yellow appearance. The skin of the face was full of tumors and scales and gave a velvety feeling when touched. The upper edge gradually merged with the normal skin of the scalp. The entire skin from neck to knees presented diffused and irregularly outlined, faintly yellowish-brown plaques, free of scales, with extremely vague outlines, and a few areas of healthy skin between, distinctly resembling parapsoriasis en plaque. The lower

part of the legs, especially of the right, presented a series of plaques and tumors. The tumors varied in size from that of barley-corn grains above the right popliteal space to several inches in diameter on the calf. The right lower leg presented a widespread violaceous plaque which involved most of it. There was no definite anesthesia or marked enlargement of the ulnar nerves. The occipital nerves were not palpable. The patient's sexual power was not reduced. The buccal mucosa was not involved. The Wassermann reaction was negative, with alcoholic antigen and + with cholesterinized antigen. A biopsy was made on one of the tumors on the right lower leg, and Dr. Highman made a histologic diagnosis of leprosy. *Lepra bacilli* were seen in the section, confirming the histologic picture.

DISCUSSION

DR. ABRAMOWITZ said he believed that the case was a nodular type of Hansen's disease.

DR. WISE said that the man was a Russian, referred by Dr. Foerster of Milwaukee, and had lived in the United States for eighteen years. The reason they had hesitated about the diagnosis of leprosy was that no anesthesia was discovered by the usual routine tests, though it might be found by a careful neurologic examination. It might be interesting to the Section to know that Dr. Fordyce had diagnosed the case as leprosy only a few days before presentation.

DR. LEVIN said that before accepting the diagnosis of leprosy the histopathology should be known and a search made for *lepra bacilli* in the tubercles. Other possibilities were parapsoriasis, mycosis fungoides, leukemia and sarcoma. Against the diagnosis of parapsoriasis were the presence of tubercles and the elevated, infiltrated, well-defined borders of the patches; against mycosis fungoides were the absence of itching and the color. A blood count and further investigation were necessary to rule out leukemia.

Last year Dr. Levin had presented a case of Kaposi's sarcoma showing tubercles resembling those on the leg in this case, and flat infiltrating patches, but with a more purplish color and not a russet as in this case. He leaned more to a diagnosis of Kaposi's sarcoma than to any other diagnosis.

DR. KINGSBURY thought that it was probably a case of leprosy, but that a diagnosis could not be made until determined by a biopsy.

DR. OCHS agreed with Dr. Kingsbury.

DARIER'S DISEASE. Presented by DR. ABRAMOWITZ.

Frank T., 24 years of age, American born and single, was referred to Dr. Fordyce's clinic by Dr. Thornley. His eruption started about two years previously while with the American Expeditionary Forces in France. He presented on the back and sides of the scalp isolated keratitic follicles the size of a pinhead. The entire interscapular region presented an inverted triangular area of used and isolated follicular keratoses. In addition, the extensor aspect of the arms and forearms showed a scattered follicular scaling. The diagnosis was confirmed by biopsy.

LICHEN NITIDUS. Presented by DR. PAROUNAGIAN.

Z. M., a Greek "bus boy," 19 years old and single, had been presented before the Section in October, 1920, and the case reported in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* in January, 1921. He had first noticed the lesions

about a year previously. When first presented, they consisted of minute shining papules, more pronounced on the flexor surfaces and most noticeable on the chest, back and genitals. There had never been any itching. The Wassermann reaction was + on Aug. 2, 1920, and was negative on Sept. 28, 1920. Between Aug. 2, 1920, and Jan. 13, 1921, he was given ten doses of arsphenamin in order to discover whether the skin condition would be influenced. On Feb. 15, 1921, his Wassermann reaction was again negative.

The lesions had improved remarkably since his first presentation.

In reply to an inquiry, Dr. Parounagian said that the patient had been kept under observation during the summer and given a placebo, and at last not knowing what to do, he was given arsphenamin in small doses, after which he improved gradually but steadily until he was almost entirely free of lesions.

DISCUSSION

DR. WISE said that the case was an interesting one. The man had had a distinct eruption of lichen nitidus when shown before. He understood that the condition had entirely disappeared as the result of treatment with arsphenamin. If that were true, it was most interesting, since pathologists generally considered the condition to be tuberculous in nature. The question was whether arsphenamin had actually caused the disappearance of the lesions on the shaft of the penis.

TERTIARY SYPHILIS. LEUKOPLAKIA. IODIN ERUPTION. Presented by Drs. PAROUNAGIAN and RULISON.

G. di. F., 41 years old, an Italian glovemaker, came to America eighteen years ago, and was under treatment at the Department of Syphilology, Bellevue Hospital. He was married twenty-two years ago, and had no children.

Twenty-six years before he had had a chancre at the frenum, and was treated with injections of mercury at intervals for twelve or fourteen years. He stated that he had received over 100 injections. Fourteen years ago he developed a gluteal abscess or gumma, which he attributed to an infected needle. This abscess left a sinus, which persisted until his first treatment here, when it healed.

The patient complained of tremor of both legs, general pain and weakness and also of headaches and pain in the left eye.

His Wassermann reaction had been tested at Columbia Hospital on Jan. 14, 1921, and was found to be + + + +. The Bellevue Hospital test of March 22, 1921, was also + + + +.

The patient on admission presented a rash on the chest and back which was due to the ingestion of iodids. The medicine was discontinued and the rash disappeared. His inguinal and right epitrochlear glands were normal. He also had leukoplakia of the dorsum of the tongue, of both cheeks and an especially thickened pea-sized patch on the center of the lower lip.

He was given one dose of neo-arsphenamin on March 24, another on March 29 and a third on March 31.

FORDYCE'S DISEASE. Presented by Drs. PAROUNAGIAN and RULISON.

W. R., an American mechanic, 22 years of age, was admitted to the clinic at Bellevue Hospital in October, 1920, for treatment of secondary syphilis. At presentation, he had no syphilitic lesions, and his Wassermann reaction was

negative. He was presented on account of the xanthoma-like deposits under the mucous membrane of the upper lip. The patient stated that he did not know how long the lesions had existed.

DERMATITIS EXFOLIATIVA. Presented by DR. LEVIN.

L. K., a Russian, aged 62, a presser of cloaks, complained of a generalized pruritus of three weeks' duration. There was no history of a previously existing eruption. Four years prior to presentation, however, he had suffered from a similar condition of the skin, which disappeared after five weeks. Drugs had not been ingested. Constipation was severe. The skin showed a universal erythroderma with scaling. The erythema was brightest on the face, where there was a moderate edema. The exfoliation occurred in the form of fine scales, except on the palms and soles where the epidermis came away in large thick shreds. The underlying skin was smooth, red and shiny. There was no evidence of eczema, psoriasis or drug application. No signs or symptoms of leukemia or tuberculosis were found.

The blood showed a white blood cell count of 10,600, and the differential count was: polymorphonuclear cells, 78 per cent., and mononuclear cells, 22 per cent.; hemoglobin, 60 per cent.

LICHEN PLANUS AND POMPHOLYX OF THE HANDS. Presented by DR. LEVIN.

M. L., aged 52, a Russian by birth and a cloakmaker, was first seen about four weeks prior to presentation. At that time, he complained of itching and blisters of the hands, and showed numerous deep-seated pinhead to lentil-sized firm vesicles with serous contents. On his return to the clinic a week later, besides the vesicles on the hands, there was a papular eruption on the hands, wrists, penis and mucous membrane of the cheeks.

When presented, the palms showed deep-seated firm vesicles and torn vesicles with collarettes of epidermis. On the palms, dorsa of the hands, the wrists and glans penis, there were numerous polyhedral, umbilicated, shiny, scaly, violaceous, angular-based papules, varying in size from that of a pea to that of a pinpoint. Grouped papules were visible on the mucous membrane of the cheeks.

ZOSTERIFORM LICHEN PLANUS OF THE BODY. Presented by DR. ABRAMOWITZ.

Mrs. M. K., 48 years of age, American born, was from Dr. Fordyce's clinic. The eruption started about three months ago, appearing first on the tongue, which showed profuse pinhead-sized, pearly white plaques on its surface. The buccal mucosa also showed the typical pearly white streaks. Isolated and grouped violaceous papules were present on the wrists and flanks, the arrangement on the left flank being like that of an extensive zoster.

MULTIPLE SPECIFIC ARTHRITIS. Presented by DRs. PAROUNAGIAN and RULISON.

M. Q., an American saleswoman, 51 years old and single, was under treatment at the Department of Syphilology, Bellevue Hospital. No primary lesion had ever been noticed; secondary infections had occurred six years before. She took medicine by mouth for a few weeks, but ceased treatment as soon as her symptoms disappeared.

For about one year her right knee had been swollen. Six months ago her left knee was affected in the same way. Her Wassermann reaction was ++++ on Feb. 23, 1921. She was given six doses of silver arsphenamin and her general condition improved. The arthritis remained uninfluenced.

The reflexes were normal on admission. Both knee joints were swollen and painful on walking. The clinical diagnosis of Charcot's joint (early) was made.

The roentgen-ray diagnosis excluded Charcot's joint and classed the lesions as atrophic osteo-arthritis of both knee joints.

MULTIPLE ARTHRITIS. TERTIARY SYPHILIS. Presented by Drs. PAROUNAGIAN and RULISON.

M. W., from the Department of Syphilology at Bellevue Hospital, was a laundress, 44 years old, who was born in the British West Indies and had lived in America for twelve years. She was married at the age of 18, and her first two children were living and well. A third child was born alive, but died at the age of 2 weeks of "snuffles," and a fourth child was stillborn. A fifth pregnancy terminated normally, and the child was living and well. Her husband died fourteen years ago, after being ill for nine months with malarial fever.

The patient said that she had injured her left knee when she was a young girl and had had more or less trouble with it ever since. Six months ago she began to have joint pains involving both knees, both shoulders, the wrists and the ankles. The pains were much worse at night. There had been no swelling except that the left knee had always been swollen at intervals since childhood.

Her Wassermann reaction, taken at the Forty-Second Street Hospital before coming to Bellevue, was + + + +. The blood test taken at Bellevue Hospital March 22, 1921, was negative. She complained of headaches, joint pains and stiffness. She had a marked Romberg sign; patellar and biceps reflexes were absent; she had sluggish triceps, and the pupils were equal and round and reacted sluggishly to light and accommodation. There was a slight haziness of the corneas.

The roentgenologic diagnosis was: "No evidence of abnormality of the distal half of the radius or ulna metacarpels. The outer half of the joint space of the right knee is increased in width. The articular surfaces are regular. There are hypertrophic, osteo-arthritic changes of the extremities of the femur and tibia. There is evidence of destruction of a portion of the inner condyle of the femur which suggests the presence of gouty tophi."

ANAL CHANCERE. Presented by Drs. PAROUNAGIAN and RULISON.

W. R., from the Department of Syphilology at Bellevue Hospital, was an American longshoreman, 26 years of age. He had lived with another longshoreman for a period of three weeks, beginning seven weeks ago. During this time, both men were drunk on several occasions. He denied any knowledge of abnormal sexual practices by his room-mate.

One month ago he noticed a slight itching and discomfort in the anal region. Seven days ago, the lower chain of inguinal glands began to swell. The upper inguinal glands of the left side were also moderately enlarged. Six days ago he developed a generalized maculopapular rash, generally distributed over the entire body. The throat was normal. The Wassermann reaction March 31, 1921, was + + + +. Two dark-field examinations were negative. On April 5 a right inguinal gland ruptured.

The patient received two doses of silver arsphenamin: March 31, 0.15 gm., and April 4, 0.20 gm., and his condition was greatly improved.

IMPETIGO BULLOSA. Presented by DR. LEVIN.

S. R., a girl, aged 2, presented a painful eruption of four weeks' duration. The lower half of the face, the hands and the diaper region were covered by large patches of denuded skin. Scattered over these areas were numerous bullous pustules as well as new pea-sized to pigeon-egg-sized bullae containing serous fluid, having flaccid walls, and situated on inflammatory bases. Several bullae had been torn and presented moist and crusted floors.

BROMODERMA TUBEROSUM. Presented by DR. OCHS.

J. D., aged 14, born in the United States, was given triple bromids, 15 grains by mouth three times daily for four weeks, with the hope that it might relieve his stammering. When he came to the Lebanon dispensary six weeks ago he presented an ulceration the size of a hazelnut on his left shin and two smaller ones on the right shin. The ulcers appeared on a noninflammatory base and bore a close resemblance to syphilis. A Wassermann test was negative. Within a few days, however, the lesions began to vegetate and the mass rose one fourth of an inch above the surface. The vegetating mass soon broke down again and left behind a somewhat punched-out ulcer. The latter condition persisted to the time of presentation.

PAUL E. BECHET, Secretary.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Stated Meeting, May 3, 1921

HOWARD FOX, M.D., *Chairman*

PROCAIN DERMATITIS. Presented by DR. HIGHMAN.

In presenting this case, Dr. Highman stated that as a cutaneous condition it was of no interest; it was a dermatitis venenata. The patient was a physician who had used procain persistently for one year. The eruption was characteristic of nothing in particular except that it was keratotic rather than vesicular and highly pruritic.

A diagnosis of dermatitis from procain was made, and various skin tests were made to confirm the diagnosis. The test, when positive, did not seem to cause a wheal. After the substance was rubbed into the abrasion, there was at first a blanching anywhere from one-quarter to three-quarters inch around it, and from twelve to twenty-four hours later a patch of vesicular and itching dermatitis would develop.

Dr. Highman said that this was only the second time he had tried this reaction, though he had had three cases of this sort. Often in procain dermatitis there was an affection of the nails which caused the skin to peel back fanwise under the nail, producing a picture very much like tinea of the nails. The treatment was simple—the use of rubber gloves so that the procain would not come into contact with the skin for two or three weeks. Involution could be hastened by the use of roentgen rays if necessary.

DISCUSSION

DR. LAPOWSKI said that he had had under his care many patients who were using different preparations, one of whom had been using dichloramin-T. The lesions appeared not only on the fingers but often patches of vesicles, sometimes of papulo-erythematous-desquamative form, were seen on the fingers, hands and face. The tests should not be applied to the affected arm but to some part of the body removed from the affected region in order to ascertain whether the same reaction would take place. The eruption could be made to disappear, but after using the objectionable preparation it would again reappear. It was not advisable to use the roentgen ray on any lesion which had a tendency to return.

DR. WILLIAMS said that it was a very interesting case. These eruptions of external origin were assuming more importance as they were recognized to be external dermatitis instead of eczema, as they were formerly called. It would be interesting to see what would happen if Dr. Highman would rub procain into the skin of a number of normal men. Such an experiment would show whether the skin of these patients had become sensitized to procain by constant handling of the drug.

DR. J. V. KLAUDER (Philadelphia) said that since the cutaneous tests had been in vogue their use had been extended not only in establishing sensitization to proteins but in determining the cause of dermatitis due to a variety of nonprotein substances. He had recently seen a physician who developed a dermatitis of the hands when in contact with arsphenamin or neo-arsphenamin. In this case a positive cutaneous test was obtained by the scarification method, employing a 1 per cent. solution of the drug.

DR. POLLITZER asked how far the condition was due to sensitization and how far the cutaneous tests were analogous to those in which there was a food product which had undergone changes in the digestive tract or in circulating blood. The tests seemed to be a demonstration of the sensitiveness of the skin to a particular poison and could not be called a cutaneous test any more than one could so designate rubbing poison-ivy leaf on a person who was sensitive to that poison. It was not analogous to a positive protein sensitization test, which implied an allergic state. In regard to the lesion itself, that was produced by the application to the scarified skin; the blanching of the skin was probably the effect of the epinephrin that was always put in these solutions. That point might be worth noting.

DR. ABRAMOWITZ, referring to the specificity of the procain skin reaction, said that Dr. Lane of New Haven had published some observations on this form of dermatitis in the March issue of the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY*. In a dentist subject to this form of dermatitis, he obtained a positive skin reaction at the site of scarification and also in places where some of the test solution (procain) had accidentally been spilled. This, together with the cure of the dermatitis after protection against this drug, was convincing evidence of the specificity of the skin reaction.

DR. HIGHMAN said he did not think a test of this sort, employed with an inorganic matter like procain, indicated allergy in the restricted sense. The test was not made to prove an abstract scientific point, but it was obvious that some skins responded pathologically to certain drugs and others did not; the cause of the skin response was hypersusceptibility or susceptibility, or idiosyncrasy to a certain drug substance. If one suspected a certain drug of causing dermatitis, and by traumatizing the skin and rubbing in that substance

caused a similar eruption, an etiologic corroboration had been elicited; a test, within certain limits, had been established. He had tried this test in two cases, and in both the characteristic eruption was produced—not a wheal, that was purely traumatic—but an erythematopapular dermatitis. The test in this case had been made the previous day.

Dr. Highman said he had seen all the various phases of the disease which Dr. Lapowski described. He was misled by the first case, and thought it was *tinca*. This patient dropped the tablet in the palm of his right hand in making his solution, and just at that site a squamous lesion developed. As for regarding all dentists with dermatitis as having procain susceptibility, he had done so in one instance, but the patient declared he had never used procain. As a matter of fact that patient had used dichloramin-T.

CASE FOR DIAGNOSIS. Presented by DR. LAPOWSKI.

C. A., an Italian woman, aged 51, a houseworker, had been married for thirty-two years and had had eleven pregnancies; the first three children died in early infancy, two in babyhood, and six were living. The causes of death of the three were not known.

Thirty-nine years ago "erysipelas" developed on the patient's forehead, leaving a scar. Six months prior to presentation she had been operated on for removal of a uterine tumor.

The eruption presented appeared five years ago, beginning as a red spot near the left corner of the mouth and gradually spreading to the localization shown. The last patch appeared alongside the right eye six months ago. There was a sensation of itching and burning. The eruption consisted of (a) miliary papules, (b) larger papulotubercles, and (c) a large plaque, slightly infiltrated and sharply defined, occupying the region of the chin and lower portion of the cheek. The papulotubercles were arranged in annular and semi-annular form, some of them conglomerated in one patch (above the external corner of the right eye and lower edge of the right jaw) which was soft, erythematous, and on diascopic pressure presented a brownish pigmentation with deep miliary points scattered and in bunches. Above the right eye was a longitudinal scar, white and slightly deeper than the surface of the skin. The origin and age of the scar could not be ascertained. The whole face and part of the forehead were occupied with the papulotubercles, which were soft to the touch—some of them dark brown, some of them pale and raised above the skin and covered with thin scales. On the anterior surface of the neck were scattered papulotubercles, some arranged in large annular formations, some disseminated. There were no ulcerations. There was a slight pruritus, but no marks of scratching.

The patient came to the clinic twenty-four hours prior to presentation, and no detailed examination had been undertaken.

On the first aspect in daylight, the lesions looked like papulotubercular syphilid, but owing to the persistence of the same lesions without undergoing any changes during five years, the likely diagnosis of syphilis was abandoned.

Dr. Lapowski suggested the diagnosis of benign multiple sarcoid of Boeck.

DISCUSSION

DR. WISE offered a tentative diagnosis of pseudoxanthoma elasticum, on account of the apparent translucency of some of the lesions as seen by poor artificial illumination.

DR. POLLITZER said that it was impossible to make a diagnosis without further data, and that nothing was to be gained by guessing.

DR. HIGHMAN said he had nothing to add except to protect his impression that the case might be in that wide group of which so little was known, the lymphoderma group, that is, pseudoleukemia or mycosis, etc. The woman had said something about itching, but since she spoke only Italian it was difficult to understand her. Whereas in most itching dermatoses one saw scratching effects, often in cases of pseudoleukemia and mycosis with itching he had not noticed them. The color and the type of infiltration made it seem probable that the condition was one of the lymphodermas. He agreed with Dr. Pollitzer, however, that any diagnosis at present was largely a matter of guesswork.

DR. WILLIAMS directed attention to one symptom that had not been mentioned—there were distinctly palpable masses above the internal condyle of each elbow. These might be enlarged epitrochlear glands, which would accord with a diagnosis of leukemia; or they might be enlargements of the ulnar nerve, which would accord with a diagnosis of leprosy. It was certainly true that one could not make a diagnosis in such a case without a biopsy, but the more that could be gained by clinical observation the better.

DR. LAPOWSKI said that what Dr. Williams had suggested about the swelling nerve trunk in the elbow region had been noted by one of the physicians who suggested the possibility of leprosy. He emphasized the presence of the milium brownish points when pressed with a diascopé to support his diagnosis of benign multiple sarcoid. Further, he said he could not agree with the suggestion of Dr. Pollitzer that one was not able to make a tentative diagnosis without further examination, since dermatologists should endeavor to arrive at a diagnosis of a case from the clinical facts—from the aspect and cause of the lesions—and only have recourse to other methods in support of the clinical findings.

URTICARIA PIGMENTOSA IN AN ADULT. Presented by DR. HOWARD Fox.

I. S., 37 years old, was a married woman, born in Russia. Her menses were established at the age of 13 and had always been regular. She was the mother of two apparently healthy children. She had had a half dozen miscarriages, most of them about the third month. Two years ago she gave birth to a dead child at full term. With the exception of severe chronic constipation, she had always enjoyed good health. She complained of considerable annoyance from a sensation of burning or itching, not severe enough to produce excoriations. She denied any knowledge of infection with venereal disease.

The eruption first appeared about ten years previously and had gradually increased up to the present time. It consisted of a large number of discrete pinhead to pea-sized macules of a yellowish brownish color. They were situated on the neck, upper third of the back, outer aspect of the arms and backs of the hands, the flexors of the forearms, buttocks, and antero-internal aspect of the thighs. The palms were free. The patient stated that none of the lesions, to her knowledge, had ever disappeared. They became markedly urticarial on friction, a fact of which the patient was well aware. She was a woman of medium height, weighing 156 pounds. The result of the biopsy and Wassermann reaction had not been reported.

DISCUSSION

DR. HIGHMAN did not think the patient had urticaria pigmentosa. The condition was more like what the French described as papular urticaria with pigmentation, which was probably a different clinical entity. One could not make a diagnosis of urticaria pigmentosa in such a case without finding mast cells at some stage in the development of the papule. As Hartzell had mentioned, in the stage of involution even typical urticaria pigmentosa might not show mast cells, and unless one could submit a slide in this case of a developing papule showing mast cells he did not think one could accept the adult case as urticaria pigmentosa. He suggested this as a caution in formulating concepts of dermatoses of this variety.

DR. LAPOWSKI said that one might call the condition urticaria with pigmentations, for that was a passing form. He had known this patient for six years, during which time she had exhibited the same lesions. In collecting with care the past histories of such patients, one usually obtained corroborations in the forms of past outbreaks of urticaria and itching to support the diagnosis of urticaria pigmentosa.

DR. WISE said that Dr. Highman's remarks were very pertinent, but he believed that cases of urticaria pigmentosa beginning in adult life are now and then encountered, exhibiting mast cells on section.

DERMATITIS HERPETIFORMIS. Presented by DR. LAPOWSKI.

L. L., 35 years of age, and married, was born in Russia and was a houseworker. Both her family and past history were negative. The first attack occurred three years previously on the body and face; the second attack occurred one year previously, two years after the first one, with severer manifestations than the first attack, larger bullae and vesicles covering nearly the entire body, accompanied by severe itching. She entered Mount Sinai Hospital where she was treated with one intravenous and several intramuscular injections of what was probably arsenic. The eruption disappeared.

Six months ago she came to the dispensary with a third attack, showing (1) scattered scratched papulotubercles on the face, shoulders, buttocks and thighs, symmetrically arranged; (2) on the trunk, especially around the sacral region and back, were pigmented areas, surrounding patches of skin in which were visible many pea-sized scars. The mucous membranes were free.

She was treated with injections of neo-arsphenamin and mercuric chlorid. During the course of the treatment, large bullae appeared on the palms and soles, symmetrically arranged, and papulotubercles over various portions of the body.

HYDROA AESTIVALE. Presented by DR. WISE.

S. G., a boy aged 7, born in the United States and in good general health, presented himself at the Vanderbilt clinic with an eruption which consisted of a few deep-seated isolated vesicles of two weeks' duration, confined to the ears. These lesions were pruritic. This was the patient's second attack. The first attack occurred last spring and persisted until the fall.

DISCUSSION

DR. BECHET did not doubt the correctness of the tentative diagnosis. He had recently observed a frank case of hydroa vacciniiforme at the Bellevue

clinic, in which the patient had typical lesions on the face and varioliform scarring from previous outbreaks. The active lesions on the ears in his case were exactly similar to those in Dr. Wise's case.

EPIDERMOLYSIS BULLOSA. Presented by DR. GILMOUR.

J. B., an Italian, 23 years old and married, had a negative family history. Since the age of 3, blisters had appeared on the hands and feet. Those on the feet appeared only in the summer (May to September, inclusive). The blisters often came on the hands, and there was a definite history of trauma noted. One-half hour of ironing a week previously caused several blisters to appear on the right hand. These were out of proportion to the pressure exerted. Blisters had not appeared on the backs of the hands or other exposed places. No scarring or pigmentation had been left. On the day of presentation, small blisters appeared without apparent cause on the palmar surface of the right little finger. For the past three days blisters had been present on the bottom of the big toe and the one next to it. The diameter as presented was three-quarters inch. An associated keratosis pilaris of the limbs was present.

DISCUSSION

DR. HIGHMAN asked whether Dr. Williams did not consider this a case of epidermophytosis or tinea.

DR. WILLIAMS replied that he thought it was not, for the reason that blisters which occur in tinea of the toes or hands were generally deep, not superficial; instead of rupturing easily, they ruptured with great difficulty in the early stages. These, on the other hand, were superficial, such as seen in epidermolysis or pemphigus. The vesicles of tinea were almost always small, and any large ones were formed by confluence of many small ones. He would rule out tinea in this case.

DR. WISE did not think the case was epidermolysis bullosa because of the lack of the little epidermal cysts which every case showed. He would like to have some one familiar with French literature express an opinion as to the diagnosis of acrodermatitis hiemalis in this patient.

DR. GILMOUR said that against the diagnosis of epidermophytosis was the fact that the blisters came out suddenly. One had appeared on the finger that day. None of those on the feet were over three days old, and some were less than that. He asked for suggestions as to treatment. No pigmentation or scarring was present.

UNIVERSAL ALOPECIA. Presented by DR. GILMOUR.

P. S., an Italian, aged 35, married, a moulder, was the father of a child with a similar condition, presented at the same time.

For a period extending over three months there had been a gradual loss of hair, which became total. This began nine years ago, and since that time there had been a complete loss of hair.

ALOPECIA AREATA. Presented by DR. GILMOUR.

G. S., a schoolboy, 8 years of age, was the son of the preceding patient.

There had been a complete alopecia of the scalp for one year. The lashes on the right eyelid had been absent for nine months; those of the left eyelid were still present.

SPOROTRICHOSIS. Presented by DR. WISE.

K. S., aged 33, an Armenian by birth, had been in the United States only a few months, and had been working as a brass polisher. He presented himself at the Vanderbilt clinic with a dime-sized papular lesion of two months' duration on the dorsum of the right hand. The lesion was ulcerated at the center and was surrounded by a wide area of erythema. There were also numerous pea-sized subcutaneous nodules, extending from the wrist to the shoulder. These nodules were rather hard and showed no signs of breaking down. The lesion on the dorsum of the hand began as a small pea-sized papule which grew larger, unattended by pain. Cultures and a biopsy were taken, but the results had not yet been reported.

DISCUSSION

DR. HIGHMAN said that the case was probably sporotrichosis, though it might possibly be blastomycosis.

GRANULOMA ANNULARE. Presented by DR. WILLIAMS.

M. C., a man aged 23, about one year previously had a small flat papule at the base of the first finger of the left hand, which was quickly followed by the appearance of about twelve others in the immediate vicinity, the entire group occupying an area of about 1½ inches in diameter. At the same time, a single lesion appeared on the back of the right hand, also at the base of the first finger. The individual lesions were soft, circular, discrete, yellowish-pink in color; some were distinctly annular with a depressed center, while others had only a slight umbilication in the center. There was no itching and the lesions had not spread, and they had grown little, if at all, since their first appearance.

LICHEN PLANUS. Presented by DR. WILLIAMS.

G. K., in August, 1920, had had a lesion on his upper lip, which he described as a cold sore, but which did not crust over as an ordinary cold sore would and which persisted for a long time. In about one month, a similar lesion appeared on the lower lip. As time went on, the lesions became less elevated and were rather flat, the lips having the appearance of being chapped. There was slight itching. The condition was treated at various clinics, and the patient was shown before several society meetings where the diagnosis was considered to be either lichen planus or lupus erythematosus. The patient was treated with sodium arsenate internally and salicylic acid salve externally, with no improvement. He stated that under roentgen-ray treatment there was a marked temporary improvement, but this soon relapsed while the roentgen-ray treatment was still being given. About a month ago several small papular lesions appeared on the backs of both hands and one on the penis. These lesions were discrete flat-topped papules with abrupt sides, rather circular in shape and bluish pink in color. The lesion on the penis was of the same nature, and there was little or no itching.

FRAMBESIFORM SYPHILID. Presented by DR. WILLIAMS.

G. D., 36 years old, was a butcher on the sea, sailing between New York and Hamburg. He had not been in the tropics. Eight weeks ago, while being shaved in a barber shop, he was cut by the barber. He later noticed three

small growths appearing on his chin. These growths rapidly attained the size exhibited and then remained stationary. Three months ago, or about five weeks prior to the appearance of the lesions, the patient had a sore on the penis, which was diagnosed as herpes. It was treated with dusting powder and disappeared in about two weeks, leaving a small scar. When presented, the patient had one large lesion below the left corner of his mouth, which was about three-eighths inch in diameter and consisted of a raised verrucous patch which two weeks before was covered with a slight crust. There were two or three similar but smaller lesions in the vicinity. There were several small scratched lesions on the scalp.

The treatment had consisted of boric acid ointment and two injections of silver arsphenamin, one a week ago, and a second on the day of presentation. The Wassermann reaction was + + + +.

DR. WILLIAMS said that the man first came to the hospital two weeks previously and presented then the picture shown tonight, except that the lesions were more elevated and warty. The lesion on the left angle of the mouth was covered with exudation and had very much the appearance of blastomycosis or tuberculosis verrucosa; it was not like the ordinary syphilid—but the man had a + + + + Wassermann reaction and a history of chancre; he also had a small pustule on the scalp, which Dr. Lapowski claimed was characteristic. In Crocker's textbook a similar case was described, the patient having a few lesions on the face and a chancre a few months later, with other eruptions on the body. Ehrlich's diagnostic atlas contained a colored plate showing almost the same lesion on the cheek. Several of the men who had just seen this case said that if the man had been seen in the tropics a diagnosis of yaws would have been made. J. Hutchinson reported a case of a man from Ceylon who contracted syphilis in London and presented a secondary eruption like yaws. This case seemed to be a secondary syphilid. Some of the textbooks did not mention it; others said it was uncommon.

DISCUSSION

DR. KLAUDER (Philadelphia) said that it was difficult on purely clinical evidence to differentiate yaws from a frambesiform syphilid. The lesions in this case bore a close resemblance to yaws; on the other hand, one could not gainsay the diagnosis of syphilis. Further study would be necessary in order to establish the diagnosis, and he believed that such study would show the case to be yaws. The laboratory diagnosis between yaws and syphilis was not easy. The diagnosis could not be made with certainty by the Wassermann reaction, although this reaction performed with an extract of yaws' nodule as an antigen might be of help in differential diagnosis. In a recent study of a case of yaws, by Dr. Schamberg and himself, morphologic differences between *Spirochaeta pertenuis* and *Spirochaeta pallida* were observed in stained specimens, although under the dark field these organisms were undistinguishable. The differential diagnosis was difficult to make by rabbit inoculations of the two organisms. The lesions of both yaws and syphilis disappeared after the administration of arsphenamin; hence the diagnosis could not be made in this manner. If the Wassermann reaction became negative after a few injections of arsphenamin, the diagnosis of yaws was favored, whereas in syphilis it was likely that many more injections would be required to make the Wassermann reaction negative. The only satisfactory way of making a laboratory diagnosis between yaws and syphilis was by a crossed inoculation of a monkey's eyebrow. If the spirochetes obtained from this case

were inoculated in one eyebrow of a monkey and after a positive result was obtained the other eyebrow was inoculated with spirochetes known to be pallida, a positive result would make the diagnosis of yaws. In other words, monkeys infected with yaws did not become immune to syphilis. On the other hand, a successful inoculation of a monkey's eyebrow with syphilis precluded obtaining a second successful inoculation with syphilis soon after the first one.

DR. HIGHMAN said that Dr. Klauder's points were well taken. Yaws seldom started except on exposed areas. In this case, the primary sore had been penile, favoring syphilis. Microscopically, in syphilis the parasites were pre-vaillingly found deep; in yaws, in the epiderm; while in yaws even more plasma cells were found than in syphilis. These data, together with the fact that after all syphilis might clinically look like this, though rarely, substantiated Dr. Williams' interpretation of the case.

DERMATITIS MEDICAMENTOSA — PHENOLPHTHALEIN. Presented by DR. CHARGIN.

Y. R., 58 years of age, married and a laborer, had a history which dated back six weeks, at which time there appeared an eruption scattered over the body, following the ingestion of four tablets of "Rexall's Orderlies," a preparation containing 1 grain of phenolphthalein per tablet. The onset was sudden, and the eruption was round, erythemato-pigmented—the individual lesions varying in size from that of a ten-cent piece to areas larger than a silver dollar. On ceasing the use of the drug the eruption involuted, leaving, however, pigmented circular areas—the pigmentation being more marked at the center than at the periphery of the individual lesions. Resumption of the remedy, even a single tablet, resulted in the recurrence of the original lesions and the appearance of new ones. At the time of presentation the patient showed the erythemato-pigmented areas in the various stages of involution. The eruption was to be noted on the forehead and neck, at the hair margins, the concha of left ear, anterior aspects of the arms, back of the chest, abdomen, sacral region, buttocks, genito-crural region and outer part of the legs.

DERMATITIS MEDICAMENTOSA (ARSPHENAMIN). Presented by DR. CHARGIN.

M. M., 34 years of age, married, and a clothing presser was the subject of cerebrospinal syphilis and had been under treatment for several years. In the course of treatment, in addition to mercury, he had received twenty-seven arspenamin injections. With the exception of an occasional secondary reaction, the patient experienced no ill effects from the arspenamin administrations. Beginning with the twentieth and following subsequent injections he had been developing a fixed erythemato-pigmented eruption, limited to the right cheek and upper aspect of the left thigh. The lesion of the cheek covered an area larger than a silver dollar, whereas the patch on the thigh was the size of a ten-cent piece. There were no other lesions. Following each injection of arspenamin after about five to six hours, the original erythematous areas lighted up again, and in the course of time the erythema gradually disappeared leaving pigmented areas similar in all respects to a mild phenolphthalein eruption. This was the second case of this type that had come under Dr. Chargin's observation, the first one having been reported in the *Journal of Cutaneous Diseases* 37:622, 1919.

XANTHELASMOIDEA. Presented by DR. GILMOUR.

M. L., aged 3½ years, born in the United States, at the age of 3 months had a red macular rash on the abdomen. This gradually spread and covered the entire trunk and limbs. The face remained free. The rash gradually became darker. Itching occurred only in hot weather. There was no eruption of the nodular type.

PAPULONECROTIC TUBERCULID. Presented by DR. OCHS.

Mrs. M. W., 33 years old, born in Hungary, had suffered from an eruption for the past nine years, at no time being free from the disease. It consisted of both superficial and discrete papulopustules which were elevated and eventually left scars. The color varied from a slight pink to a deep red. Active lesions and scars were most numerous on the legs, a few being present on the arms, chest and upper part of the back. They occasioned no subjective symptoms. The diagnosis of a papulonecrotic tuberculid had been confirmed by a biopsy. The Wassermann reaction was negative. The patient was also suffering from a marked polycythemia (Vaquez' disease). The hemoglobin varied at different times from 120 to 158 per cent., and the red cells from 9,500,000 to 10,900,000. The white cell count was 10,200.

DISCUSSION

DR. POLLITZER expressed some doubt as to whether the condition was a papulonecrotic tuberculid and suggested that it might be a papular prurigo-leukemia. The blood count, of course, was peculiar but might more or less fit in with a leukemic disturbance. The red blood count was tremendously high, and one suspected that something was wrong when it was stated that 10,000,000 red blood cells were counted in blood from the finger tip and 7,500,000 in blood taken from another point at the same time; certainly the circulating blood did not differ so greatly in different parts of the body. The white blood cells could not be regarded as increased in view of the polycythemia. It was unfortunate that no differential count had been made.

DR. LAPOWSKI said that clinically the case did not look like a tuberculid. The lesions on the arm resembled more a pruriginous papule, and the erythematous-urticarial patch on the chest, with itching, would support Dr. Pollitzer's suggestion.

DR. WISE said he had had an opportunity to examine the slide and it looked like a tuberculid, not a granuloma. Histologically, the diagnosis of tuberculid was more likely than prurigo. Whether or not there was any relation between a tuberculid and polycythemia was to be considered, but his impression was that the skin disease and the polycythemia were not related, and that the patient had two conditions. So far as he could remember, the slide showed an inflammatory reaction in the corium, evidences of necrosis, with ordinary inflammatory cellular exudates so commonly seen in biopsies of papulonecrotic tuberculids.

DR. HIGHMAN, referring to Dr. Wise's remarks, said that the histologic report was not enough to base a diagnosis of tuberculid on. To begin with, we are still confused as to the standard morphology of tuberculids. They show various pictures. One cannot make a diagnosis of tuberculid histologically unless something suggesting tuberculosis is seen. The fact that nothing but lymphocytes were seen would not indicate tuberculid more than leukemia or pseudoleukemia.

DR. HOWARD FOX said that the intense itching of which Dr. Ochs had spoken would be an indication against the diagnosis of papulonecrotic tuberculid.

GRANULOMA INGUINALE. Presented by DR. ROSEN.

J. H., a mulatto, 23 years of age, a porter, born in the United States, presented a deep, crusted, sharply bordered ulcer in the right inguinal region, measuring $2\frac{1}{2}$ by $1\frac{1}{2}$ inches. It had existed for two years. No *Spirochaeta pallida*, but numerous other spirochetes, had been found. A biopsy and culture were made, the results of which will be reported later.

DISCUSSION

DR. KLAUDER said he did not think there was any doubt as to the diagnosis, since he thought the lesions were typical of granuloma inguinale. The finding of spirochetes on the surface of the lesions should not complicate matters, since it was not remarkable to find a variety of spirochetes on any ulcerating surface.

DR. WILLIAMS agreed with the diagnosis.

DR. WISE regretted that Dr. Klauder's diagnosis was not confirmed microscopically. Dr. Teague, who examined the lesion bacteriologically, was unable to find Leishmann-Donovan organisms in the scrapings and tissues, nor were tubercle bacilli discovered.

DR. HERMAN GOODMAN said that he had been able to demonstrate the causative organism in three out of four cases seen in the tropics. The method he had found to yield the best results was that of using tissue smears. The surface of the lesion was cleansed and a portion of the active margin removed. The portion cut was then trimmed so that only deep tissue was available. This was washed in saline, expressed, and smears were made. In this manner, no superficial contaminating organisms were present to cause confusion.

After he had advised this procedure, the organisms had been demonstrated in a patient on Dr. Clifton's service at the New York Skin and Cancer Hospital. Only that afternoon he had carried out the procedure on a patient on Dr. Parounagian's service at Bellevue Hospital, and the organisms were demonstrated. Previous examinations of tissue and smears had not been successful.

There had been some difference of opinion as to the bacterial agent of the condition. There had been confirmatory evidence accumulating for the two main contenders, namely, for the Calimato-bacterium granulomatis origin, and this was the organism demonstrated in the three hospital cases under his observation, and the spirochete aboriginalis origin. This organism was demonstrated in the fourth of his cases. It was certain that this spirochete was neither the *S. pallida* nor the *S. refringens*.

In four other tropical cases that he had seen but not studied intensively, the organisms had not been demonstrated.

He had made bacteriologic studies of tissue from the patient presented at the December, 1920, meeting of the Section (*Arch. Dermat. & Syph.* 3:331, 1920). Dr. Stein had been kind enough to furnish this material at operation, but he had not succeeded in demonstrating the organisms in that case.

PAUL E. BECHET, Secretary.

SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MADRID

*Regular Meeting, May 4, 1921*Dr. Azúa, *Presiding*

SILVER ARSPHENAMIN AND MALTA FEVER. Dr. BERTOLOTY.

Dr. Bertoloty had two patients with Malta fever who had been treated with all the usual measures without any success. He tried silver arsphenamin with such good results that he considered it his duty to report the fact to the society, since the cure was complete.

DISCUSSION

Dr. SAINZ DE AJA added to the two cases Dr. Bertoloty reported, one more in which arsphenamin had been used. After the first injection the fever cycle disappeared; then recidivation occurred. More arsphenamin was administered, and the patient recovered completely.

SERPIGINOUS ULCER. Presented by Dr. COVISA.

The patient had already been presented in previous sessions. As no relief was obtained with local treatment, Dr. Covisa recalling Criado's patient who recovered after tuberculin treatment, applied this agent. After the first injections she improved remarkably. The treatment was stopped, and the patient grew worse. Tuberculin was tried again, and now the patient is almost entirely well. Two patients with cases of the same nature have therefore been cured; this seems to be important.

Dr. CRIADO did not consider this a mere coincidence. He recalled that in his case the serpiginous lesion healed before the tuberculous gummae.

Dr. SAINZ DE AJA said he was interested in knowing why these patients recovered after tuberculin treatment. In his opinion, there occurred a tuberculinization of the lesions which might suggest why they became serpiginous-venereal on the surface and tuberculous at the bottom.

Dr. Azúa said that it was not known what serpigo was. Therefore it might be considered venereal in origin without being so. He mentioned six cases in which great improvement was noted in the patient after the administration of potassium iodid. Apparently the presence of Ducrey's bacillus is not necessary in a serpiginous lesion. Dr. Azúa thought that in the two cases of Criado and Covisa a definite cure had been obtained with tuberculin by chance, and that the lesions were tuberculous lesions of atypical forms.

Dr. COVISA considered the problem more complicated because there are doubts as to whether tuberculous lesions are cured by tuberculin and because serpiginous zones were healed before the tuberculous ones.

CASES FOR DIAGNOSIS. Presented by Dr. SAINZ DE AJA.

Two patients had almost identical ulcerated lesions of the phagedenic type, which had nearly destroyed the foreskin and had pushed their way 2 cm. below the pubic skin. In both, specific treatment had failed. Since these may be cases of venereal serpigo on a chancre base they will be treated with tartar emetic. The patients were presented so that they might be examined before treatment.

ALOPECIA AREATA AND SYPHILIS. DR. SANZ DE GRADO.

Several cases of pelade are reported in which a careful examination disclosed syphilis. Therefore Dr. Sanz de Grado thought that in view of the theories of the French school a like investigation must be made of all patients with pelade.

DR. SAINZ DE AJA said he had discussed on another occasion the lack of relationship between pelade and syphilis. In the cases in which he had seen this association, pelade patches had never healed with specific treatment.

DR. COVISA stated he had not seen a relationship between both conditions but out of regard for Sabouraud's views it should be either confirmed or disproved.

DR. GIMENO agreed with Dr. Sainz de Aja, saying he had looked for syphilis in his patients, and in most of them he could not find it.

DR. AZÚA did not believe that there was any relationship between alopecia areata and syphilis, as he had stated six years ago. This does not imply that Dr. Sanz de Grado has not reported his cases properly, and the repeated therapeutic successes justify consideration of this relation.

ONYCHOTRICHOPHYTIA. Presented by DR. GRANDE DE RIEGO.

This clinical case had been confirmed by laboratory examination, and as roentgen-ray treatment had failed, the patient will be treated with vaccines.

VARICOSE ULCER TREATED BY INTRAVENOUS INJECTIONS OF SODIUM CARBONATE. DR. FORNS.

A patient from Dr. Aja's service in San Juan de Dios Hospital had had varices in both legs for fifteen years, presenting multiple ulcers which healed and reulcerated frequently. When the patient was first observed she had had, for a long time, a superficial ulcer in the lower third internal aspect of the left leg about the size of a dollar. She was treated according to Sicard's method with injections of 5, 7, 9 and 10 c.c. The ulcer disappeared at the fourth injection, and the patient was dismissed at the end of fifteen days. The only local treatments were hot packs of permanganate.

DR. BARRIO DE MEDINA, Secretary.

**TWELFTH CONGRESS OF THE GERMAN
DERMATOLOGICAL SOCIETY**

May 15-19, 1921

A congress of about 400 specialists in skin and venereal diseases was held in Hamburg. Besides Germany, Austria, Sweden, Norway, Holland, Denmark, Finland, Czecho-Slovakia, Japan and Spain were represented.

SYPHILIS AND THE SPINAL FLUID. PROFESSOR NONNE.

Professor Nonne, the neurologist, was the first speaker. Basing his statements on fifteen years of experience, he emphasizes the necessity of making diagnosis, prognosis and treatment of pathologic spinal fluid depend on the exact control of (a) the number and species of cells, (b) spinal fluid pressure,

and (c) globulin reaction. There is generally a slight rise in spinal fluid pressure in tabes and progressive paralysis. A distinct rise is seen in syphilitic meningitis. As to lymphocytosis, 40 per cent. of all syphilitic patients show an increase of lymphocytes without showing any nerve symptoms. Nonne then pointed out differences in the development and course of tabes and progressive paralysis. He stated that progressive paralysis in exceptional cases can be cured (mentioning six of his own patients). The missing globulin reaction is the proof that cure has been effected—as the globulin reaction is seen only in true syphilitics. The Wassermann reaction was then mentioned. This is positive in all cases of tabes and progressive paralysis—generally showing a stronger reaction in the latter. A positive Wassermann reaction is not in itself an indication for treatment. Several cases were mentioned and examples given to demonstrate this. Hemolysin reaction is not considered specific for syphilis by Nonne, although this reaction is seen in both tabes and progressive paralysis. In some cases the nervous system is attacked by syphilis as early as a few months after infection. The cerebrospinal fluid, as a rule, soon becomes infectious. In spite of this, 60 per cent. of patients with primary and secondary cases of syphilis with pathologic fluid are cured. Normal cerebrospinal fluid does not prove the absence of syphilis. The speaker again emphasized the necessity of examining the cerebrospinal fluid in cases of isolated Argyll Robertson pupil in syphilitic meningitis for exact diagnoses. As to the effect of treatment on cerebrospinal fluid, good results are obtained contrary to the experience in progressive paralysis, in which the effect is only transitory. In spite of this, clinical symptoms may show rapid movement. The success of treatment will always depend mainly on the degree of infection and the strength of the defensive action of the system. In summarizing, Nonne cautions against treating diseases instead of patients, against trying reactions instead of considering the state of health of the infected person.

SYPHILIS AND THE SPINAL FLUID. DR. KYRLE.

Dr. Kyrle of Vienna said that soon after infection the cerebrospinal fluid may become pathologic. He did not believe that skin symptoms, that is, a projection of the disease into the skin, protect the spinal fluid from infection in any way. In leukoderma and alopecia specifica the speaker had often seen positive spinal fluid tests. Normal spinal fluid at the beginning of the secondary stage means little. Beyond the second year after infection, however, the spinal fluid rarely becomes positive. As for treatment, Kyrle recommends mercury and arsphenamin, especially the latter. Insufficient cures with arsphenamin are apt to cause provocation.

MERCURY COMPARED WITH ARSPHENAMIN. DR. KOLLE.

Dr. Kolle of Frankfurt described his experiments on rabbits with the numerous solutions of mercury now on the German market as compared with arsphenamin. He failed to cure the syphilis of rabbits, contrary to the experience with arsphenamin.

ABORTIVE TREATMENT OF SYPHILIS. DR. ROST.

Dr. Rost of Freiburg mentioned 882 cases of seronegative syphilis. In 736 of these there were no relapses after one year, in 305 no relapses after from one to two years, and in 319 no relapses after two years. No definite standard method of treatment was agreed on, yet on the whole the combined treatment was preferred and seemed to dominate.

RELATION OF DERMATOSES TO INTERNAL SECRETION. DR. BROCK.

Dr. Brock of Kiel pointed out the relation of dermatoses to internal secretion. He believes in the influence of the thymus gland on psoriasis. The therapeutic measures resulting herefrom (stimulating doses of roentgen rays) are a new factor in the treatment of psoriasis. Other diseases, such as lichen ruber planus, ichthyosis and ichthyosis hystrix were well influenced by this method.

METHOD OF APPLYING TURPENTINE. DR. KLINGMÜLLER.

Dr. Klingmüller of Kiel explained his method of applying turpentine. A 10 per cent. solution is given into the gluteal region in varying doses from 0.5 to 5 c.c. Klingmüller could not explain how this agent acts—he does not think that a direct influence on lesions thus treated is possible.

INJECTIONS WITH MILK. DR. MÜLLER.

Dr. Müller of Vienna, speaking of injections with milk, said that the greatest effect of these injections was obtained in transudation and hyperemia. He thinks the stronger inflammation is caused by the changes in the colloidal balance of the blood serum. From 5 to 6 c.c. are injected several times, however, not before the patient has recovered from the reaction following the preceding injection. From one to two hours after the injection the patient has chills and there is a rise in temperature—the height of which is attained within from ten to twelve hours. As to the blood, there is first leukopenia, then an increase of the leukocytes. This treatment is most successful in epididymitis, periurethritis, proctaritis, gonorrhea, buboes and affections of articulation. No effect is seen on gonorrheic urethritis and soft chancres; it is also effective in the eczemas and trichophytosis.

ANAEROBIC CULTURES OF GONOCOCCI. DR. BUSCHKE.

Dr. Buschke of Berlin explained his experiences with anaerobic cultures of gonococci (on human serum). The gonococci can be preserved for a long time although they multiply slowly. Applying his experiences to the prognosis of chronic gonorrhea, his opinion is that in many cases of gonorrhea a latent infection exists, that is, gonococci remain hidden without showing clinical symptoms. Basing his arguments on the preference gonorrhea shows for the seminal vesicles, prostate gland, etc., as well as on our inability to get at latent gonococci, Buschke is pessimistic as to our chances of curing gonorrhea.

A long discussion followed in which Gennerich, Blaschko and others expressed more optimistic views.

GONORRHEIC ULCERS. DR. FUCHS.

Dr. Fuchs said that gonorrheic ulcers are very superficial, not undermined, prone to bleed, and seldom found in women. A 10 per cent. solution of nitrate of silver destroys them.

GENESIS OF CARCINOMA CAUSED BY ARSENIC. DR. ULLMANN.

Dr. Ullmann of Vienna discussed the genesis of carcinoma caused by arsenic. The disease is practically limited to America and the British colonies on account of the high doses of arsenic given in these countries. Often furunculosis and hyperhidrosis are combined. Histologic examination showed a resemblance to ordinary carcinoma.

NEW NOMENCLATURE FOR DISEASES OF THE SKIN. DR. ROST.

Dr. Rost of Freiburg proposed a new distinction and nomenclature for the diseases of the skin. He would like to see these diseases classified according to:

(a) Lesions (external causes).

1. Specific (bacilli, etc.).
2. Chemical.
3. Physical.

(b) Dispositions (internal causes).

1. Nutritive disorders.
2. Neurogenous disorders.
3. Vascular disorders.
4. Genetic disorders.

INFLUENCE OF INTRAVENOUS INJECTIONS OF SILVER ON GONORRHEA. DR. HEUCKY.

Dr. Heucky of Munich discussed the influence of intravenous injections of silver on gonorrhea. His experiments show that little can be expected from this method in itself unless it is combined with local treatment. The combined method cured 72 per cent. of the cases of uncomplicated gonorrhea in females. The disadvantages of using injections of silver are that headaches and giddiness are sometimes caused; also the length of treatment, as very small doses only in increasing rising concentrations can be administered. In cases of epididymitis this treatment did not prove as effective as the vaccine therapy, whereas in prostatitis it gave better results than the latter. In vulvo vaginitis infantum the results were good. In a few cases Heucky cured gonorrhea in females with silver arsphenamin.

The congress was closed by a visit to the Hospital for Tropical Diseases. A large number of interesting cases of *ulcus tropicum*, oriental sore, sporotrichoses, etc., were demonstrated.

EDWARD AHLSEWEDE, M.D., Hamburg, Germany.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, May 18, 1921

BARKER B. BEESON, M.D., *Presiding*

FOLLICULITIS AND PIGMENTATION. Presented by DRs. ORMSBY and MITCHELL.

A man, aged 24 years, was under treatment for pruritus ani and was also being treated for syphilis by another physician. On his trunk were lesions which had been present, and in the same condition, for six or seven years, consisting of areas of pigmentation, small follicular papules and minute pustules. Itching had preceded the appearance of the dermatosis. The patient denied chancre and all secondary infections, and antisypilitic treatment had had no effect on the skin lesions.

DISCUSSION

DR. FOERSTER thought a more careful examination would be necessary before he could make a diagnosis. The multiformity of the lesions, together with the pustular folliculitis which had been followed by infiltration and later by atrophy, suggested tuberculids, although the lesions were not in the usual areas. He was unable to classify the disorder in any other group.

DR. SENEAR believed tuberculid would have to be considered, but he was inclined to regard the condition as a case of chronic, low-grade folliculitis.

DR. LIEBERTHAL considered it a case of acne vulgaris.

DR. ORMSBY regarded the case as an unusual amount of pigmentation following follicular pus infections.

BLASTOMYCOSIS. Presented by DR. WAUGH.

A man, aged 38 years, whose disorder had been present for nine months, had two lesions, one covering over half of the nose and the other behind the lobe of the left ear. The lesion on the nose was distinctly papillomatous, bluish red, with some purulent secretion and a few pinhead size miliary abscesses near the margin. Blastomyces had been demonstrated microscopically. The patient had recently been discharged from the Municipal Tuberculosis Sanitarium, where he was treated for pulmonary tuberculosis.

DISCUSSION

DR. BAER thought the lesions and the organisms demonstrated under the microscope were characteristic of blastomycosis.

DR. ORMSBY thought the diagnosis lay between tuberculosis and blastomycosis, and the only possible way to demonstrate the difference between the two conditions was by demonstration of the blastomyces. He was unable to accept the organism under the microscope as that of blastomycosis.

DR. WAUGH said he had thought of tuberculosis verrucosa cutis. The case resembled that disorder to some extent. The miliary abscesses in the margin of the lesion on the nose, however, were typical of blastomycosis. He had been able on previous occasions to demonstrate typical budding blastomyces. The sputum had not been examined, and it was possible that the patient had pulmonary blastomycosis as the tubercle bacillus had not been found when the patient was in the sanatorium.

DERMATITIS HERPETIFORMIS. Presented by DR. OLIVER.

A child, aged 1½ years, presented a disorder which had been present since March, 1921, when enlarged glands in the neck had been noted. The mother had influenza in March, 1919, while pregnant.

The lesions consisted of bullae, vesicles and papules and were grouped over the scalp, face, arms, back, buttocks, legs and face. Marked itching was present. The condition responded promptly to the administration of Fowler's solution.

DISCUSSION

DR. PUSEY thought it was a case of dermatitis herpetiformis.

DR. MICHELSON thought it probably had been a case of multiform erythema, because of the rapid development and rapid involution of the lesions.

DR. OLIVER called attention to the fact that the mother had had influenza during the gestation of this child, and that the baby had always been nervous. He had considered the diagnosis of erythema multiforme on account of the multiform character of the lesions, but the intense itching, the grouping and the response to arsenical therapy led him to regard the case as one of dermatitis herpetiformis.

CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

A woman, aged 38 years, whose trouble began on the nose about five months ago, was seen at the University of Illinois in February, at which time the entire lower two thirds of the nose was bright red, enlarged, and presented a papillomatous appearance, with some discrete pustules. Tertiary syphilis, severe acne rosacea and blastomycosis had to be considered. Examination of the pus disclosed sporelike bodies, some of them budding. Despite the fact that neither the clinical picture nor the organisms were typical of blastomycosis, the patient was given potassium iodid, and the eruption cleared up within two or three weeks. Within a short time there was a recurrence, and the potassium iodid was then without effect. It was stopped after a short time as the condition seemed to become worse.

DISCUSSION

DR. FOERSTER thought the case might have been one of blastomycosis at the onset, but that the lesions now looked like an ulcerated nodular syphilid.

DR. QUINN agreed with Dr. Foerster.

DR. SENEAR said he did not intend to give the impression that a diagnosis of blastomycosis had been made when the case was first seen. He was not sure about the organism under the microscope. The Wassermann reaction was negative. The present eruption had not responded to potassium iodid, and he was afraid to continue that drug because of the possibility of increasing the pustular element. No mercury or arsphenamin had been administered.

DR. PUSEY thought the lesions on the nose were probably not due to potassium iodid and believed mercury and potassium should be given a fair trial before abandoning the diagnosis of syphilis.

DR. ORMSBY stated that he saw this patient on one occasion in January, 1921. At that time he made a diagnosis of rosacea with an acute dermatitis due to the application of an irritating ointment. The patient was in a belligerent mood and was planning to sue a druggist for improperly filling a prescription. At the present time the lesions so closely resembled a syphilid that he felt there was no doubt about the diagnosis. He advised the use of arsphenamin.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DRS. ORMSBY and MITCHELL.

A woman, aged 56 years, injured her hand in October, 1920, and later developed a lesion near the site of injury. Her son had recently died of pulmonary tuberculosis, and she had nursed him throughout his illness. The lesion began as a small nodule at the base of the right thumb, on the dorsal surface, and gradually enlarged. At the time of presentation this was a dollar-sized, well defined, slightly elevated, crusted, erythematous lesion. A

small crusted lesion was present on the flexor side of the wrist, and there were thickened patches on the left shin near the shoetop, which were said to have been present for years. The scalp was clear.

The patient was under treatment with roentgen therapy.

DISCUSSION

DR. PUSEY regarded the case as a beautiful example of tuberculosis verrucosa cutis.

DR. ORMSBY said the case was typical and thought it was interesting on account of the rapid progress of the infection.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

The patient was a man, aged 28 years, who was first shown before the society in 1917 by Dr. Harris. At the age of 3 years he had a bullous eruption which persisted until he was 16, when it disappeared. This disorder recurred a year and a half ago and has persisted since that time. The lesions were grouped, and itching was intense. In association with this he had developed a brownish desquamation in the axillary folds, the bends of the elbows, on the abdomen and elsewhere at points of friction or pressure. When shown in 1917 the patient presented only the latter type of lesion. Acanthosis nigricans and ichthyosis were considered as diagnoses at that time.

The previous report appeared in the *Journal of Cutaneous Diseases* 36:245, 1918.

DISCUSSION

DR. ZEISLER regarded the case as one of dermatitis herpetiformis followed by pigmentation.

DR. PUSEY said that in his opinion it was not a simple pigmentation. In the axilla there were verrucous lesions and papillary hypertrophy. He was unable to accept the diagnosis of dermatitis herpetiformis with pigmentation, and believed the only condition which resembled it was acanthosis nigricans. He was beginning to believe that acanthosis nigricans was probably a loose sort of entity—concerning whose course there was a good deal to be learned; he recalled a case that he had demonstrated before the society twenty years ago, which had almost completely cleared up.

DR. FOERSTER said the skin was of the ichthyotic type about the ears, backs of the hands and arms, and believed it might be a case of ichthyosis hystrix with dermatitis herpetiformis.

DR. SENEAR said that when this patient was shown in 1917 he had had a period of freedom from the bullous manifestation of the disease for four years. He had seen the patient recently during an acute stage of the eruption. He had reconsidered the diagnosis of ichthyosis and acanthosis nigricans for the scaly and pigmented part of the eruption. The vesicular eruption comes on rapidly and involutes rapidly; the lesions are grouped and itch severely.

LICHEN PLANUS. Presented by DRs. ORMSBY and MITCHELL.

The patient was a practicing physician, aged 54 years. The first attack occurred eight years ago and cleared up with tar preparations. He remained free from the eruption for three years, when a less severe attack occurred which disappeared soon after the lesions had been cauterized. Three years ago he had had another severe attack which lasted only a few weeks and in

which the eruption had been cleared up by protiodid of mercury. The lesions were situated chiefly on the backs of the hands, with some on the legs and abdomen. For the last four or five months he had had lesions of the same areas, but also some of a different type. Two or three months ago small red patches of raised epidermis appeared here and there. These could be easily rubbed off, without scratching, and this was followed by bleeding. Large, confluent areas covered the greater part of the ulnar surface of both legs, and in these areas erosions had occurred in several places. Typical lichen planus papules were present on the forearms and scrotum, as well as on the buccal mucous membrane. Nikolsky's sign was present. The patient had diabetes and high blood pressure, and there was some anasarca of the legs.

DISCUSSION

DR. BAER thought the lesions were typical of those of lichen planus.

DR. EISENSTAEDT said the lesions on the wrist were characteristic of lichen planus. The unusual feature of the case was the presence of Nikolsky's sign, which he had not noted heretofore in this disease.

DR. PUSEY thought that the ease with which the epidermis could be removed in this case amounted to the presence of Nikolsky's sign. He was unable to accept this as pathognomonic of pemphigus. Some years ago he saw the sign present in an erythematous and papular multiform erythema, and since he had observed it in a number of different dermatoses. He thought the explanation was, in this case as in others, that there was an exudation sufficient to produce a loosening of the corneous layer but not sufficient to produce the formation of vesicles. This was an instance of Nikolsky's sign in lichen planus.

DR. MICHELSON said he had seen two cases of lichen planus occurring in physicians, and in both instances the patients had resorted to irritating applications rather than to submit to intramuscular injections. He believed this case was probably similar to the ones he had seen, and that the external applications probably had injured the epidermis to the point of producing what appeared to be Nikolsky's sign.

DR. ORMSBY said that the patient was now receiving intramuscular injections of mercuric chlorid. He agreed with Dr. Pusey in regard to Nikolsky's sign. Some years ago he saw a patient with lichen planus who had bullous lesions on the legs, but he had taken no arsenic. In this case the lesions were not classic but abortive bullae.

LINGUA NIGRA. Presented by DR. WAUGH.

The patient was a colored man, aged 30 years. The disorder had been present for five months and involved most of the dorsal surface of the tongue. The condition of the anterior third of the involved area had been practically cleared up with radium treatment.

DISCUSSION

DR. SENEAR was much interested in the results obtained by the radium therapy.

DR. PUSEY was anxious to know whether the lesions removed by radium would recur. If they did recur, he thought the advisability of again removing them with radium was doubtful. He believed it would be better to have the lesions on the tongue than to produce radium changes in it.

DERMATITIS HERPETIFORMIS. Presented by DR. ZEISLER.

The patient was a boy, aged 12 years, whose disorder had been present for three years. The lesions were scattered over the scalp, face and body, and he was unable to sleep because of the intense itching and burning. Marked photophobia was present. At the time of presentation there were grouped macules and dried vesicles, which were situated chiefly on the trunk. The Wassermann test was negative. A blood count showed an eosinophilia of 8 per cent.

DISCUSSION

DR. BAER agreed with the diagnosis of dermatitis herpetiformis but was unable to say what connection the photophobia might have with the dermatosis.

DR. FOERSTER thought the presence of scleral and conjunctival lesions would account for the photophobia, and asked whether such lesions were present.

DR. ZEISLER said he had observed definite vesicles and wheals. The patient was receiving arsenic and was improving rapidly. The grouping of the lesions was a pronounced feature of the dermatosis.

LUPUS ERYTHEMATOSUS OF THE LIP. Presented by DR. LIEBERTHAL.

This patient was demonstrated at the January, 1921, meeting of the Chicago Dermatological Society (*Arch. Dermat. & Syph.* **3**:674 [May] 1921). At that time the reaction following radium therapy had not subsided. The patient was shown again to demonstrate the results of radium therapy.

SYRINGO-CYST ADENOMA. Presented by DRS. ORMSBY and MITCHELL.

The patient was a girl, aged 17 years, who had had the disorder for about four years. It began in the fall as what she thought was "prickly heat," and had not spread since first noticed.

The lesions were grouped on the sides of the neck and upper chest and consisted of round and oval, light brown, slightly elevated match-head to pea-sized nodules, about 100 in all. This area sometimes becomes very red; itching occurs periodically and is intense for a minute or two. Dermographism was slight.

DISCUSSION

DR. PUSEY said he now had a patient with lesions similar to these. The clinical picture and the sections in his case constituted a replica of the case reported by White.

DR. FOERSTER believed this disorder is probably much more frequent than the number of cases reported would indicate. He had often seen single discrete lesions in patients under examination for other disorders.

DR. LIEBERTHAL said he demonstrated a typical case before the society several years ago, but the microscopic picture was not that of a syringo-cyst adenoma, and there were none of the characteristic findings of that disorder present.

DR. SENEAR wished to know whether radiotherapy was giving results in this case. The late Dr. Shaffner had obtained such excellent results from this method of treatment in the case he showed several years ago. In the first biopsy made in their case only a few adenomas were shown, but in the subsequent biopsy they found the characteristic changes.

DR. ORMSBY said that in this case the clinical diagnosis had been made when the patient was first seen. No attempt had been made to secure a biopsy because of the disposition of the patient. The case differed from the one he reported some years previously under the title syringoma in that the lesions in that case were extensive and the sweat function had entirely ceased. The lesions subsequently cleared up and sweating was restored. The histology in that case showed what appeared to be typical benign epithelioma. There was marked epithelial hypertrophy of the coils. The patient recovered entirely after the use of roentgen therapy.

FOLLICULITIS DECALVANS. Presented by DR. OLIVER.

A man, aged 26 years, presented lesions in the scalp which began in October, 1912, and which had persisted despite treatment ever since. Papules, papulo-pustules and considerable alopecia were present. He complained of itching and burning.

DISCUSSION

DR. LIEBERTHAL had first thought of favus in this case. The patient was American born of Polish parents and, therefore, might have acquired the disease from Polish born relatives or friends. The lesions were not typical of favus but were sufficiently suggestive to warrant search for the achorion. He believed the diagnosis lay between favus and folliculitis decalvans, with the probability of the latter being the correct one.

DR. FOERSTER found that the scars were granular and not smooth and depressed as in favus. He felt quite sure the case was one of folliculitis decalvans.

DR. OLIVER was glad to have the suggestion in regard to favus and said he would make a careful examination for the achorion. He regarded the case as one of folliculitis decalvans.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

The patient was a girl, aged 17 years, who complained of redness of the face which had been present for about eight months. It was said to have developed over night.

The cheeks showed a diffuse, sharply outlined erythema, covered with very fine, adherent scales. Soothing applications had been used locally without effect.

DISCUSSION

DR. PUSEY said the symmetry, the scaling and a slight increase in the thickness of the skin in the areas involved suggested a superficial lupus erythematosus.

DR. LIEBERTHAL agreed with Dr. Pusey's diagnosis. He thought the description of erythema centrifugum fitted the case—a diffuse form of the disease.

DR. SENEAR was struck by the close resemblance of the face in this case to that in the man who was shown with lupus erythematosus by Dr. Waugh. He had not observed the atrophy in the lesions until it was pointed out to him by Dr. Foerster. He agreed with the diagnosis of Dr. Pusey.

LICHEN PLANUS HYPERTROPHICUS. Presented by DR. ZEISLER.

The patient, a man aged 42 years, had had the lesion on the internal surface of the right leg for two years. He worked with cyanid of potassium, to which he attributed the disorder.

The lesions occupied the entire inner surface of the right leg from the knee to the ankle. They were confluent, shiny, purplish-red, somewhat verrucous plaques. Intense itching was present.

DISCUSSION

DR. QUINN was unable to make a diagnosis.

DR. PUSEY said it was a queer case of a queer disease; namely, lichen planus.

DR. ZEISLER agreed with Dr. Pusey.

A CASE FOR DIAGNOSIS. Presented by DRs. ORMSBY and MITCHELL.

The patient was a man, aged 39 years, whose trouble began in September, 1917, as blisters on the abdomen about the belt line. Other lesions appeared later on the nose and ears and in the scalp, and scattered over the body, grouped between the shoulders. Remissions had occurred, but the disorder had never entirely cleared up. No vesicles had been seen, but Nikolsky's sign has been constantly present. Crusting had been present since the time of onset. No subjective sensations were present. One brother had had pulmonary tuberculosis. Exacerbations of rather severe character had occurred twice yearly in spite of treatment. All blood examinations had been negative. No biopsy had been made.

DISCUSSION

DR. FOERSTER thought the duration of three and a half years, the lack of response to treatment and the peculiar uniformity of the lesions suggested a benign form of pemphigus.

DR. PUSEY summarized the salient features of the case as follows: The man had a patch on the nose which was red and almost weeping, and there were numerous seborrheic patches on the forehead. He also had a great deal of dandruff of the scalp. He thought Hebra's form of lupus erythematosus, which Hebra called seborrhea congestiva, fitted the picture in this case. He was unable to see how one could get away from that diagnosis. The duration and lack of response to treatment suggested lupus erythematosus. He was not ready to offer a diagnosis as to the patches on the body.

DR. LIEBERTHAL thought the greasy character of the patches suggested the diagnosis of seborrhea, and believed that the appearance of the lesion over the nose and cheeks might be in part due to external applications.

DR. ORMSBY said that when the patient was first seen there were crusted lesions on the chest and back. At that time there were only a few lesions on the nose, but gradually and almost imperceptibly the lesions spread. The erythematous condition of the lesions now was probably in part due to the recent removal of the crust by the use of ointment. The patient had received intensive internal treatment with mercury and arsenic, but the disorder had progressed in spite of the internal and external treatment. The patient stated that he had vesicles from time to time, but Dr. Ormsby had never been able to find them. The case was different from any he had hitherto seen. The description of lupus erythematosus on the face fitted the lesions exactly. The lesions on the body had resembled seborrheic dermatitis, but salicylic and sulphur ointment was without any appreciable effect. The disorder had the therapeutic rebelliousness of lupus erythematosus and the appearance of seborrheic dermatitis.

A CASE FOR DIAGNOSIS. Presented by DR. OLIVER.

The patient was a colored man, aged 25 years, who had lesions on the tongue which had been present for the past four months. They were not painful and had been little influenced by treatment. The patient had had a chancre four years ago. He had recently received five injections of neoarsphenamin. The Wassermann reaction was negative.

DISCUSSION

DR. BAER considered this case one of geographic tongue.

DR. LIEBERTHAL agreed with Dr. Baer.

DR. QUINN also agreed with Dr. Baer.

DR. ORMSBY thought the lesions were multiple benign plaques, and said he had treated a number of such cases with radium with excellent results.

Book Reviews

DERMATOLOGY. THE ESSENTIALS OF CUTANEOUS MEDICINE.
By WALTER JAMES HIGHMAN, M.D. Cloth. Price, \$6. Pp. 482, with 95
illustrations. New York: Macmillan Company, 1921.

Highman states in his preface that another reference book of dermatology would have no justification, and that his volume "aims to present essentials succinctly, consecutively, completely and simply, without sacrificing important detail." The contents therefore include "the author's conception of the minimum requisite for an adequate outline of the subject." In addition he has attempted to handle the subject, "so far as practicable, from the standpoint of internal medicine" emphasizing the beliefs connected with the interrelation of skin diseases and internal medicine.

It is true that with so many excellent texts of dermatology already available, a new treatise should have some special features to justify its existence, and it seems to the reviewer that Highman's text meets this requirement. Bibliography, histologic descriptions, and historical sketches, all of importance in the larger reference books, have been sacrificed in order to present to the novice or general practitioner only those things which are essential. The descriptions of the symptoms of the various diseases deal chiefly only with the characteristic pictures, although the variations are never slighted, but mentioned briefly—usually in fine print. The sections on differential diagnosis are excellent, the various differential points being detailed so fully as to be of great value to the inexperienced.

The discussion on etiology and pathogenesis, while complete, dismisses many theories with a word, but gives fully those which have impressed the author as being important. It is in these discussions that particular attention has been given to the inter-relation of dermatoses and the physical economy as a whole, and Highman presents clearly the pros and cons of the various theories.

In discussing the treatment of the various disorders, the author includes only those methods which have commended themselves to him. The reader has, therefore, no large list of therapeutic aids to select from, but those given are well chosen, furnish an adequate armamentarium, and their value is greatly enhanced by the frequent detailed discussion of their indications and the methods of employing them.

A valuable feature of the book is the frequent use of classifications, giving the reader a survey of the clinical or etiologic relationships of many diseases; the chart of nevi on page 354, and that of multicellular animal parasites on page 223 are illustrations of this.

In following out his policy of giving special attention to internal medicine, Highman has included a comprehensive section dealing with the cutaneous manifestation accompanying various general disorders, such as typhoid, typhus, pertussis, mumps, etc.

The illustrations, while they number only ninety-five, are all in plate form, and are selected to illustrate well the more common cutaneous disorders. The legends accompanying the illustrations are detailed, usually giving a short résumé of the main points in the condition pictured, and pointing out those features which are illustrated. In one instance the text and the legend do not agree, however, as in discussing pompholyx he states that it is "associated with

a disturbance of the sweat secretion," while the legend of Figure 16 states that "there is no real association with sweat disturbance."

The book is replete with expressions of the author's opinions on many points, and while not all will agree that pityriasis rosea "is clearly infectious," that dermatitis herpetiformis and pemphigus are so closely related as possibly to destroy the former as a clinical entity, etc., it is always made clear that these are disputed points. The discussion of the questionable duality of eczema and simple dermatitis, that of the term "precancerous" and other topics serve to show the usual decisive opinions of the author.

The text can be recommended to the beginner and those inexperienced in dermatology—for whom the author states that it was intended—as a valuable aid in the recognition and treatment of cutaneous diseases, while it will help them to understand more clearly that dermatoses are frequently only the outward expressions of more general disorders. Those more experienced in dermatology will also find much to interest them in the up-to-date exposition of this aspect of their specialty.

AN ATLAS OF THE PRIMARY AND CUTANEOUS LESIONS OF ACQUIRED SYPHILIS IN THE MALE. By CHARLES F. WHITE, O.B.E., M.B., Major, Royal Army Medical Corps; Lecturer on Venereal Diseases and Officer in Charge of the Rochester Row Military Hospital; and W. HERBERT BROWN, M.D., Physician for Diseases of the Skin, Victoria Infirmary, Glasgow; Late Captain, Royal Army Medical Corps (T.C.); with a Foreword by LIEUT.-GEN. SIR T. H. J. C. GOODWIN, K.C.B., C.M.G., D.S.O., K.H.P., Director-General, Army Medical Service. New York: William Wood and Company. 1920.

This small quarto with thirty-three pages of text, seventy-nine illustrations in black and white and about twenty illustrations in color is an effort to salvage some of the extensive experience in venereal diseases obtained in a large army hospital during the war. Its production represents a commendable spirit, and one approaches the book with predilections in its favor. The text, while brief is clear, concise and comprehensive. The authors have succeeded well in the brief space at their disposal in summarizing a great experience. The illustrations in color, while not numerous, are good. Neither the English nor we are as yet able to produce as good colored pictures as are produced in continental Europe, particularly in Germany, but these colored pictures are well up to the best standard of English or American production. Some imperfection in the coloring of the colored pictures is not a great defect in the reviewer's estimation, for colored pictures are not as useful as black and white illustrations of skin diseases unless they represent the colors perfectly, and that is excessively rare. The halftones made from photographs are excellent. They are well selected, illustrate most of the manifestations of syphilis of the surface, and are sharp and clear. The photographs are all stereoscopic and are produced in duplicate, and, examined with a stereoscope, they show the lesions remarkably well.

The one criticism to be made of the book is the price—\$9.00. The prices of English books at present are often excessive. This monograph is a well illustrated chapter on cutaneous syphilis. Except for the stereoscopic feature, these illustrations are no better and are not much more numerous than will be found in articles on syphilis in standard works. Nine dollars is too large a price for such a production.

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Archives of Dermatology and Syphilology

VOLUME 4

SEPTEMBER, 1921

NUMBER 3

RESEARCH PROBLEMS IN DERMATOLOGY*

JAY FRANK SCHAMBERG, M.D.

PHILADELPHIA

Fellows of the American Dermatological Association:

It is my pleasant duty to bid you welcome and to announce formally the opening of the scientific sessions of the American Dermatological Association.

Your president is charged with the traditional duty of addressing the members of this body on some topic of general dermatologic interest. The forty-three preceding addresses have so fully covered the field that it is difficult to present a text that is either new or important.

It might not be unprofitable, however, to discuss briefly certain phases of our knowledge, or lack of knowledge, of the etiology of a few diseases of the skin, to which special interest attaches. These furnish problems for research which it is to be hoped will be attacked and solved by present and future members of this and similar bodies.

Nature conceals many of her secrets so well that only the most persistent and intelligent effort is permitted to dispel the heavy veil of obscurity which envelops them. Like the trick of the magician, what is apparently unfathomable, becomes diaphanously simple when the solution is known.

Scabies was a mysterious disease before it was definitely ascertained that it was caused by the itch mite and by this parasite alone.

Our successors may speak with condescending tolerance of the day when the causes of pityriasis rosea, lichen planus, psoriasis, acne and other common dermatoses were the subjects of unfruitful discussion. Such, however, is the history of the various sciences, and we need not feel undue humiliation in admitting the facts. The consciousness of our deficiencies, however, should stimulate us to labor energetically to shed every possible illumination on the hitherto unascertained causes of diseases of the skin. Contributions to our knowledge of diseases of the skin may, by analogy or otherwise, aid in the elucidation of the etiology of deeper seated affections.

*Presidential address read before the forty-fourth annual session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

CANCER

Do not the reasonably demonstrated causes of cancer of the skin, point as far as they go against the parasitism of cancer? Let us briefly appraise our evidence. That the chemical or actinic rays of light are a factor of importance in the causation of cancer of the skin can scarcely be doubted. Sailors and farmers, who are perhaps more exposed to the sun's rays than persons in other occupations, exhibit the highest incidence of cancer of the face and hands. I have seen many thousands of negroes with skin diseases, but I have yet to observe a full-blooded negro with keratosis or cancer of the skin of the face.¹ The pronounced layer of pigment appears to act as an effective barrier against the ingress of the noxious actinic rays. Certain other forms of radiant energy—the roentgen rays and radium rays—may under certain conditions produce cancer of the skin. The relationship of the effect of the solar and roentgen rays is perhaps best illustrated in that distressing and remarkable disease known as xeroderma pigmentosum. When we mention the sequence of the cutaneous phenomena—freckle-like pigmentation, dryness, atrophy, telangiectases, keratoses and malignant neoplasms—do we not conjure up the picture of chronic roentgen-ray effects? The disease is familial but not hereditary. As many as seven boys in a single family consisting of eight boys and five girls have been reported by Ruder to suffer from this disease. It would certainly appear that these children exhibit a congenital hypersensitivity to the action of the actinic rays of light. To them is not the sun virtually a huge roentgen-ray tube, exposure to which produces progressive changes leading to cancer and ultimately death? The study of the causes of this hypersusceptibility offers an important field for research. Toyama, after a study of thirty-three cases in Japan, declares his belief that the prevalence of the disease in that country is due to intermarriage. Vignolo-Lutati likewise expresses the opinion that the predisposition of the cutaneous cells results from consanguinity.² Other causes of cancer of the skin worthy of further investigation are: the long continued and excessive ingestion of arsenic and the influence of long continued external exposure to tar, soot and crude paraffin.

Dermatologic experience indicates that cancer of the skin is in the vast majority of cases (omitting possibly the cancers developing from

1. I have seen one case of cancer of the face in a negro, but the subject was an elderly mulatto.

2. It may be here remarked that there is another disease in which there exists a hypersensitivity to the sun's rays, although the effects are quite different. In pellagra, inflammatory changes occur in the skin under the influence of solar rays which are insufficient to evoke such effects in normal persons. The cause here is presumably a biochemical one.

nevi and similar growths) due to repeated mechanical, chemical and actinic or electromagnetic stimuli. The causes that render persons hypersusceptible to these influences is a fertile field for investigation.

ACNE

Another dermatosis of absorbing interest is the common affection—acne. Concurrent clinical experience furnishes certain definite data concerning the predisposing cause of this affection and certain factors which provoke outbreaks, but who is there that can make an authoritative pronouncement on the complex etiologic relationships? In general terms, acne is a disease of puberty and of the decade following its inauguration. A few years ago, while examining several hundred medical students for demobilization, I was astounded to find that approximately 70 per cent. of the young men had more or less acne on the trunk. The statement has been generally accepted that the development of acne is coincident with the physiologic activity of the pilosebaceous apparatus that accompanies puberty. This is regarded, however, as a predisposing cause and other factors are believed to be operative to produce a sufficient perversion of the physiologic process to result in actual disease. Various contributory causes are cited by all authors, chief among which are disturbances of the alimentary and utero-ovarian systems.

Most writers believe the exciting cause to be bacterial and interest has focused on the bacillus described by Sabouraud, Unna and Hodara, Engman, and Gilchrist. As the microbacillus of Sabouraud may, however, be found in myriads in the sebaceous material expressed from the follicles of the nose of practically all adolescents and adults, it is possible that this organism is merely a saprophyte under ordinary conditions and becomes noxious only in a soil prepared by other factors. The staphylococcus is certainly not the cause of acne, and yet it is present in all acne pustules.

General experience will support the statement that practically all young female patients with acne exhibit a menstrual exacerbation of the eruption. Less well authenticated but asserted by many experienced clinicians is the allegation that masturbation and other sexual stimulation in young men is provocative of acne outbreaks.

When the phenomena of the menstrual acne relapse is considered in conjunction with the initial onset of acne at the approach of puberty, the inference appears to be justified, in the light of modern studies on endocrinology, that an internal secretion from the sex glands or of some other endocrine structure energized by the gonads is an etiologic factor of importance. May not the ovarian or testicular hormone or hormones of correlated organs of internal secretion overstimulate the sebaceous glands and alone or associated with other factors lead to the

development of acne lesions? To be sure, acne lesions commonly develop from other causes in the interim between the menstrual periods, but the monthly outbreak is nevertheless striking. It is also suggestive that after the cessation of ovarian activity—in other words after the menopause—acne is practically unknown.

THE INFLUENCE OF ENDOCRINE GLANDS ON THE SKIN

Endocrinous glands may have a stimulating influence on similar glands elsewhere, or they may exert an antagonistic or repressive effect. Many disorders of the ductless glands produce profound changes in the skin and subcutaneous tissue and exert an influence either stimulating or inhibitory on the activity of the sebaceous and sweat glands.

We are all familiar with the white, dry, scaly and indurated skin of myxedema; the hairs fall out and the sebaceous and sweat secretions are suppressed. Darier says that the hypothyroidism of the menopause, which is very common, gives rise to a greatly attenuated picture of myxedema. On the other hand, in hyperthyroidism, we have by contrast the flushed moist skin seen in exophthalmic goiter.

ICHTHYOSIS

There is a not uncommon dermatosis of unknown origin and regarded by most writers as a congenital malformation in which the skin is harsh, dry and scaly, in which the sebaceous and sweat secretions are greatly diminished and in which the hairy system may be imperfectly developed; the patients are usually thin, poorly developed and of low resistance. Does not this disease, which we call ichthyosis, suggest a disturbance of the endocrine glands? Colcott Fox, Weill and others have recorded cases of ichthyosis in which there was atrophy of the thyroid gland and improvement after thyroid treatment. Winfield reported the case of an infant with ichthyosis that died at the end of two and one-half weeks and who at necropsy was found to have no thyroid gland. On the other hand, Rion described a case of fetal ichthyosis in which necropsy disclosed the presence of a normal thyroid gland.

POSSIBILITY OF AN INTERNAL SECRETION FROM THE SKIN

Despite the incompleteness of our comprehension of the relationship between the various glands of internal secretion, interlocking reciprocal influences have been demonstrated.

The thyroid stimulates the gonads or sex glands and the chromaffin system. The thymus inhibits the sex glands and its atrophy favors sexual development. The interrenal system stimulates the sex glands and is reciprocally stimulated by them. The anterior and middle portions of the pituitary stimulate the sex glands, inhibit the thyroid and are themselves inhibited by the thyroid and the sex glands.

From our knowledge of the condition of the skin in myxedema, acne and oily seborrhea, there is some reason for the assumption that the thyroid and the sex glands and possibly the pituitary gland stimulate the action of the sebaceous follicles.

The skin with its complex architecture and the numerous highly specialized structures therein contained cannot be regarded merely as the protective envelop of the body, but as an important organ whose functioning is essential to life.

Biedl includes among the organs of internal secretion the spleen, the pancreas, the gastric and intestinal mucosa and the kidneys. Is it not conceivable that there may be likewise an internal secretion from the skin, emanating possibly from the sebaceous glands or some other structure contained within the derma? That the sebaceous glands are commonly overstimulated when puberty sets in is suggested by the development of oily seborrhea at this time; it rarely if ever develops before this period. When senility is reached sebaceous secretion becomes markedly diminished. In hypothyroidism, and particularly in myxedema, the secretion of the sebaceous glands is diminished or suppressed. If there is an internal secretion from the skin the sebaceous glands would appear to be the most likely structures involved in the process on the principle that a gland of internal secretion is stimulated by one endocrine center and often repressed by another. The mechanism of secretion of the sebaceous glands is quite different from that of the excretory glands of the body. It is not merely an outpouring of a fluid as is the case with the kidneys and sweat glands; excessive sebaceous secretion is due to an abnormal cellular proliferation within the gland—the cells then undergoing fatty degeneration, the nucleus becoming contracted and ultimately disappearing and the cell wall progressively distended, thinned and ruptured. The fatty cells and detritus are then extruded into the excretory duct.

In some respects the activity of the sebaceous glands is similar to that of the mammary glands. Both structures consist of racemose glands and in each case a fatty fluid is secreted through fatty degeneration of cells.³ While the mammae are not included by most writers as glands of internal secretion, yet the effect of lactation on menstruation and on the involution of the uterus is recognized; furthermore, at the beginning of pregnancy the injection of a mammary extract augments to a remarkable degree the tonicity of the muscle fibers of the uterus.

3. The analogy between the mammary and the sebaceous glands is further suggested by an observation in natural history. There are two mammals which are believed to have survived from prehistoric times which lay eggs and do not suckle their young—the Ornithorhynchus and the Echidna. The young browse over the maternal skin and feed on a nutritive fluid which exudes from scattered glands in the skin. No mammae or nipples exist.

The mammary glands might therefore be regarded as subsidiary organs of internal secretion, and in a somewhat similar sense the sebaceous glands may occupy a parallel position.

It is admitted, of course, that the suggestion of the existence of an internal secretion from the skin is purely speculative and unsupported at the present time by any experimental evidence. Hypotheses, however, are often useful as a stimulus and guide to more accurate observation and as an incentive to research. A medical friend has suggested to me the possible value of a desiccated skin extract in ichthyosis, and I have requested a pharmaceutical laboratory to prepare a desiccated cutaneous extract of the skin of the pig for trial in this disease. I have, moreover, recently suggested the use of testicular and thyroid extract in a pronounced case that has come under my observation.

It might advance our knowledge of this affection if in ichthyotic patients coming to necropsy, a careful microscopic examination of the thyroid, gonads, pituitary and other suspected endocrine glands were made.

ECZEMA

If time permitted, one might refer to the need and opportunity for research in connection with that conglomerate concept which we call "eczema."

There is a crying need for an elucidation of the causative factors in this widespread and distressing disease. Some cases are, to be sure, merely instances of acute, subacute or chronic dermatitis—due to the action of external irritants. In some instances the external stimulus is operative only in the presence of a systemic sensitization. Many eczematoid eruptions are of mycotic origin. In the cases of chronic, relapsing and rebellious eczema various causes operating from within may be at work. It becomes the duty of the dermatologist to ascertain whether protein sensitization from food or bacteria, endocrine disturbance, focal infection, intestinal toxemia, renal insufficiency or some general metabolic disorder is the etiologic factor. The solution of these vexed questions is astoundingly difficult and often impossible, but the responsibility for their clarification rests primarily with us, and we must face the task if we are to uphold the dignity and importance of our special calling.

It is reasonable to hope and expect that within the next decade physiologic chemistry, pathologic chemistry and biochemistry will throw a much needed light on the problems involved. Our duty should be by honest and painstaking effort to speed the day when what is now unknown in dermatology shall become known in the interest of science and of humanity.

THE SACHS-GEORGI REACTION IN THE SPINAL FLUID OF PATIENTS WITH SYPHILIS*

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The Sachs-Georgi reaction depends on the visible flocculation of a cholesterinized alcoholic extract of beef heart on its incubation with specific serums or spinal fluid. Drs. Sachs and Georgi¹ in their original paper claimed a reliability equal to, or even greater than, the Wassermann reaction in distinguishing syphilitic from nonsyphilitic serums, but in a later paper they² somewhat modified this view. Several other investigators, Georgi,³ Plant,⁴ Nathan,⁵ Levinson and Petersen,⁶ Logan,⁷ with slight modifications of the original technic, report results favoring the accuracy of the reaction as an additional method for the serodiagnosis of syphilis.

In reviewing the literature, it is noted that most of the results with the Sachs-Georgi reaction are recorded on serums. As a reliable estimate of the value of the reaction can only be judged after the findings of several laboratory workers are collected, the present series of comparisons of the Sachs-Georgi and the Wassermann reactions on the spinal fluid in syphilitic cases were undertaken. The Wassermann tests on all the spinal fluids were made by Doctor Ide of the State Psychopathic Hospital, Ann Arbor, who directs such work for the University Hospital and for several other state institutions. The reading of each Sachs-Georgi reaction was made without previous knowledge of the results of the Wassermann test, and except in a few cases, each reaction was made on the same day. This permitted an unbiased opinion in noting the degree of flocculation of the Sachs-Georgi reaction, as well as a comparison with a Wassermann test conducted by a reliable and experienced laboratory worker.

* From the Department of Neurology, University of Michigan, School of Medicine, Ann Arbor, Michigan.

* The spinal fluid was obtained from the Dermatology Clinic, Dr. Udo Wile, and the Clinic for Neurology, Dr. C. D. Camp.

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The summarized results of my work in 379 cases are given in the table. The cases are classified as paresis, tabes dorsalis, latent syphilis, etc., in accordance with their clinical characteristics.

In this table of 379 cases, an absolute agreement is shown in 323, or 85 per cent., and a disagreement in 56, or 15 per cent. If, however, the cases are included that are in practical agreement, that is, doubtful vs. positive, 344, or 91 per cent., agree and 35, or 9 per cent., disagree. Further inclusion of cases in which the results are not diametrically opposed, that is, negative vs. doubtful, 360, or 95 per cent., are in agreement and nineteen, or 5 per cent., disagree. Of the nineteen cases that are at variance, three cases, two of tabes dorsalis and one of cerebrospinal syphilis, are cases in which the Wassermann test was positive and the Sachs-Georgi reaction negative. The sixteen cases in which the Sachs-Georgi reaction was positive and the Wassermann test was negative comprise one case of paresis, two cases of tabes dorsalis, one case of cerebrospinal syphilis, seven cases of latent syphilis, one case of primary syphilis, two cases of secondary syphilis, one case of tertiary syphilis-gumma and one case of vascular syphilis. Thus, the most noticeable divergence is in the earlier form of syphilis, showing no clinical symptoms or signs of central nervous system involvement. These results speak in favor of the greater sensitiveness of the Sachs-Georgi reaction, and this is especially noted on considering the cases under a given diagnosis.

In sixty-four cases of paresis, the results in fifty-eight, or 91 per cent., agree and six, or 9 per cent., were in disagreement; of the latter, four favored the Wassermann and two the Sachs-Georgi reaction. Of eighty-one cases of tabes dorsalis, seventy-one, or 88 per cent., were in absolute agreement; the ten divergent cases were equally divided. Of 104 cases of cerebrospinal syphilis, fourteen, or about 14 per cent., were not in agreement; eleven cases favored the Wassermann reaction. Eighty-four cases of latent syphilis showed a difference in results of 19 per cent.; of the sixteen divergent cases, three favored the Wassermann and thirteen the Sachs-Georgi reaction. Twelve cases of primary syphilis differed in two, or 19 per cent., being entirely in favor of the Sachs-Georgi reaction. Twelve cases of secondary syphilis diverged in three, or 25 per cent., also being in favor of the Sachs-Georgi reaction. In ten cases of tertiary syphilis-gumma—eight, or 80 per cent., were in absolute agreement, the two remaining cases being in favor of the Sachs-Georgi reaction. Of the three divergent cases of vascular syphilis, one favored the Wassermann and two the Sachs-Georgi reaction.

This tabulation would suggest that the chief interest in the flocculation reaction lies in the question of an earlier serodiagnosis of neurosyphilis than that provided by the Wassermann reaction.

Diagnosis	Number of Cases	Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- mann Reaction		Wasser- 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The general distribution of positive Sachs-Georgi readings on Wassermann negative fluids of patients with the earlier forms of syphilis would tend to rule out the query of false positive flocculation reactions.

TECHNIC

Many variations and modifications of the technic as given by Drs. Sachs and Georgi were tried before attempting the present series of cases. These experiments will be given in a later paper. The technic I used is as follows: The lipoid mixture was prepared according to the directions of Drs. Sachs and Georgi. An alcoholic extract of fresh beef heart was prepared by using 1 gm. of macerated heart muscle to 5 c.c. of 96 per cent. alcohol, which was extracted for twenty-four hours in an icebox; this was filtered, and to 100 c.c. of the filtrate 200 c.c. of 96 per cent. alcohol and 13.5 c.c. of a 1 per cent. alcoholic cholesterin solution were added. Just before the test, one part of the alcoholic extract was diluted with five parts of 0.85 per cent. NaCl solution, and the latter added slowly, resulting in a marked opalescent emulsion. To 1 c.c. of the spinal fluid was added 0.5 c.c. of the emulsion; this was incubated for twenty-four hours at 37 C. As a control, at least four tubes of 1 c.c. of 0.85% NaCl solution plus 0.5 c.c. of the emulsion were used, as well as a known positive and negative spinal fluid. The heart extract mixture was selected for sensitiveness from several tried preparations as the variations, though prepared with the same technic, were marked. All glassware used was thoroughly clean and sterile. The saline solution was sterile.

The following scale for reading the degree of flocculation was used:

Negative, no visible change in the emulsion even with the aid of a hand lens.

Doubtful, production of very small flocculi with slight clearing.

Moderately positive, not complete clearing with numerous small flocculi.

Positive, complete clearing with large flocculi adherent to the side of the tube or massed in the bottom.

In classifying, the moderately positive were recorded as positive.

CONCLUSIONS

1. The results of the Sachs-Georgi reaction on the spinal fluid closely parallel those of the Wassermann test.

2. The Sachs-Georgi reaction is a substitute or may be a valuable addition to the Wassermann test on the spinal fluid.

3. The Sachs-Georgi reaction furnishes a means for an earlier sero-diagnosis of central nervous system syphilis than the Wassermann test.

RECKLINGHAUSEN'S DISEASE: ITS RELATION TO THE ENDOCRINE SYSTEM

REPORT OF AN ILLUSTRATIVE CASE *

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Throughout this article the term "Recklinghausen's disease" is used for all cases presenting the varying syndrome usually indicated by the name "generalized neurofibromatosis." Von Recklinghausen¹ and Adrian² have both long since objected to the latter term as giving an incorrect impression of the nature of the growths characteristic of the disease. Many French physicians have also made the equally valid objection that the name "generalized neurofibroma" has thrown undue emphasis on only one aspect of the syndrome and has thus limited the disease, in the minds of many, to its most common forms, to the exclusion of the unusual and incomplete forms, "formes frustes," which are not so unusual as one is led to believe. The latter, of which the author's case is an example, almost invariably shows pigmentation, and the accompanying psychic, nervous, and trophic disorders frequently play a more important part in the life of the patient than do the cutaneous disorders themselves.

The form of Recklinghausen's disease most frequently seen is that with multiple molluscosus fibromas and neuromas, with or without pigmentation, and no obvious nervous or trophic troubles. Parkes Weber,³ in 1909 (page 52), makes this classification: (1) plexiform neuroma unaccompanied by multiple molluscosus tumors of the skin, with or without cutaneous pigmentation, (2) multiple molluscosus tumors of the skin without obvious neurofibromatosis of the nerve trunks, with or without cutaneous pigmentation, (3) pigmentation of the skin not (at least as yet) accompanied by obvious neurofibromatosis of the nerve trunks or molluscosus tumors (cutaneous neurofibroma), and (4) anomalous cases of neurofibromatosis complicated by the coexistence of bony or epidermic (papillomatous) changes. Weber and

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Little⁴ state that an early incomplete form of the disease is seen in cutaneous pigmentation (diffuse brownish café-au-lait patches or sheets of pigmentation, discrete spots and patches, lentigo, and pigmented nevi) which may be present a long time, usually in young people, frequently from birth, before any molluscous skin tumors appear. There are many cases in the literature in which melanoderma is the only cutaneous symptom of Recklinghausen's disease.

THE ADDISONIAN SYNDROME

Besides the cutaneous conditions of Recklinghausen's disease, and, significantly, particularly in those cases characterized by marked pigmentation, there is quite frequently seen a more or less complete syndrome indicative of dysfunction of the glands of internal secretion, and recalling the picture of insufficiency of the suprarenal glands in Addison's disease. This condition may include any or all of the following:

1. Sensory Disorders: Arthralgic or rheumatoid pains, general or localized particularly to the lombo-abdominal region and the calves of the legs; formications; vague esthesias; hyperesthesias.

2. Motor Disorders: Vertigoes; motor incoordinations; trepidations; augmentations of reflexes; diminution of muscular force; asthenia, sometimes progressive to death. Landowski⁵ (Thèse, Paris, 1894) states that "what dominates with these patients is a state of general depression or torpor similar to that of Addison's disease. They can hardly move themselves—walking is painful—the slightest movement is a labor. All intellectual effort is fatiguing. The face is dull and stupid, the body more or less bent, thin, and meager."

3. Psychic Symptoms: Difficulty in learning at school is most commonly mentioned; apathy, indifference; hesitations of speech, stammering; loss of memory; melancholia; fatalism; sometimes imbecility and idiocy of the cretinoid type. The adenoid facies is noted. Charpentier,⁶ 1910, states that 63 per cent. of the cases of Recklinghausen's disease are accompanied by psychic defects symptomatic of mental degeneracy. The disease is rare in veritable aliens. As is obvious, these conditions are quite different from those present in the same disease when the neurofibromatosis has invaded the cerebrospinal nerves or even the central nervous system itself; in this case, there are symptoms common to any condition of cerebrospinal pressure.

4. Little, G.: Meeting Roy. Soc. Med., Dermat. Sec., June 17, 1909, Brit. J. Dermat. **21**:253, 1909.

5. Landowski, L.: La neuro-fibromatose généralisée, Gaz. hôp., Paris **69**: 946, 1896.

6. Charpentier, J.: Maladie de Recklinghausen et psychose périodique, L'Encephale **5**:460-465, 1910.

4. Defects of Development and Faulty Nutrition: Stigmas of degeneracy usually congenital, such as nevi, arched palate, facial asymmetry, prognathism, malformation of ears, syndactylism, badly spaced teeth, troubles with the nails. The adult, usually of small stature, shows lack of complete development, infantilism, faults of the hairy system, dwarfism and sexual underdevelopment with frigidity. There is frequently scoliosis, kyphosis, osteomalacia and friability of the bones.

5. Digestive Complaints: Anorexia, nausea, cramps, vomiting.

6. Examination of the urine may reveal glycosuria and albuminuria, and the blood may show a certain degree of eosinophilia.

Few patients have all of the symptoms mentioned in the foregoing, but many possess a sufficient number of them to present an unmistakable syndrome which various French writers, notably Charpentier, call the classic picture of Recklinghausen's disease, regarding the psychic symptoms as practically habitual.

REVIEW OF THE LITERATURE⁷

A somewhat detailed account of characteristic cases is here presented, since, except in the article of Elliott and Beifeld⁸ (1914), which attempts to connect Recklinghausen's disease with the condition status thymolymphaticus, there has been no review in English of the work of many foreign writers, notably of the French and Italian, who have endeavored to establish a connection between Recklinghausen's disease and glandular dysfunction. Although many cases are reported in which the writer's interest was so entirely dermatologic as to exclude any other information, and although there are others in which the authors state that no nervous or functional symptoms were present, there is also considerable literature on cases in which involvement of the endocrines, sex glands, pituitary and thyroid glands, and suprarenals is unmistakable. The picture is one of general glandular dystrophy with varying emphasis on different glands in different cases.

Sex Glands.—It is significant that many cases, some with no particular Addisonian complex, are influenced by the onset of menstruation, by pregnancy and by the menopause. Pigmentation and tumors usually first appear or rapidly increase between the twelfth and the eighteenth years; it is quite a common statement in the histories of both male and female cases that the disease developed at the onset of puberty.

7. An excellent review of the literature up to the year 1903 may be found in Adrian's article of that year.

8. Elliott, C. A., and Beifeld, A. F.: Generalized Neuromatosis. Report of a Case Showing a Superficial Resemblance to Hodgkin's Disease. *J. A. M. A.* **63**:1358-1362, 1914.

Menstrual anomalies figure in certain cases, as in Meige and Feindel's⁹ (1903) myxedematous case of infantilism, in which menstruation was barely established, and in a similar case of Orzechowski's¹⁰ (1912) of a girl of 18 in whom it had never been established.

Bourcy and Laignel-Lavastine¹¹ (1900) reported a case in which tumors first developed at the age of 15; more appeared after marriage; and immediately after the menopause a mollusum pendulum appeared. Hirst¹² (1911) and Sutton¹³ (1914) had cases in which tumors appeared during pregnancies, but not between pregnancies. In Sutton's case, the tumors shriveled up after the first delivery, but some of those of the second pregnancy persisted.

Bérard¹⁴ (1902) reported a case without an Addisonian picture, in which an enormous cyst of the ovaries was associated with multiple cutaneous and subcutaneous tumors. After ovariectomy, the tumors progressively disappeared until at the end of three years only the smallest remained. Pascalis¹⁵ (1911) and Oddo¹⁶ (1905) report similar cases.

Many of the male cases also develop or become active at puberty, and an incomplete or delayed sexual development, cryptorchidism and lack of pubic hair and other characteristics are mentioned in cases without any other obvious signs of glandular involvement. Harbitz¹⁷ (1909) reports the case of a man of 28, who showed pigmentation at birth and developed generalized cutaneous fibromas at the age of 15. There was cryptorchidism. Bénaky¹⁸ (1904) had a patient, a man of 40, with congenital pigmentation, generalized neurofibromatosis and

9. Meige, H., and Feindel, E.: *Infantilisme myxoedémateux et maladie de Recklinghausen*, *Rev. neurol.* **11**:857, 1903.

10. Orzechowski, K., and Nowicki, W.: *Zur Pathogenese und pathologischen Anatomie der multiplen Neurofibromatose und der Sclerosis tuberosa*, *Ztschr. Neurol. u. Psychiat.* **11**:237-307, 1912.

11. Bourcy, P., and Laignel-Lavastine: *Un cas de maladie de Recklinghausen*, *Soc. méd. hôp.* **22**:21-26, 1905.

12. Hirst, B. C.: *Etiological Influence of Pregnancy on Mollusum*, *Am. J. Med. Sc.* **147**:419, 1914.

13. Sutton, R. L.: *A Clinical Note on Fibroma Mollusum Gravidarum, Fibrosum*, *Am. J. Obst.* **63**:256, 1911.

14. Bérard, L.: *Ancien kyste de l'ovaire et tumeurs cutanées multiple*, *Bull. Soc. Chir. Lyon.* **5**:15 (Nov. 13) 1902.

15. Pascalis, G.: *Mollusum pendulum volumineux de la cuisse au cours d'une maladie de Recklinghausen*, *Bull. Soc. anat. de Par.* **13**:102, 1911.

16. Oddo, C.: *Maladie de Recklinghausen avec pigmentation des muqueuses*, *Rev. neurol.* **13**:412-415, 1905.

17. Harbitz, F.: *Multiple Neurofibromatosis*, *Arch. Int. Med.* **3**:32 (Feb.) 1909.

18. Bénaky: *Neuro-fibromatose généralisée avec mollusum pendulum de la moitié droite de la face*, *Ann. de dermat. et syph.* **5**:977-982, 1904.

molluscum pendulum, with skeletal deformities, diminution of sensibility, cramps and fatigue, accompanied by sexual underdevelopment. Guinon and Reubsæt¹⁹ (1907) describe the case of a boy of 12 with pigmentation from birth, progressively growing tumors, stupidity, adenoid facies and lack of testicular development. Preiser and Davenport,²⁰ Elliott and Beifeld, Poisson and Lebat,²¹ and Graham Little report similar conditions in young boys.

Pituitary Gland.—It is to be expected that cases of Recklinghausen's disease should be associated with hypophysis dysfunction, as there seems to be some connection between hypopituitarism and certain tumor formations, apparent in conditions like multiple lipomatosis, etc.

Evidences of pituitary dysfunction in Recklinghausen's disease are found in many cases showing a partial acromegalic tendency, such as prognathism, cheironmegaly, and in the confluent elephantiasic form of the disease, as well as in the few cases in which generalized fibromas appear with outspoken acromegaly. The latter, six in number, are the cases of Feindel and Froussard²² (1899), Piollet²³ (1902), Cushing²⁴ (1912), Nicolas and Favre²⁵ (1910), de Castro²⁶ (1912), and Wolfsohn and Marcuse²⁷ (1912). The cases of the two latter (de Castro, and Wolfsohn and Marcuse) both showed typical pigmentation and generalized tumors, together with typical acromegaly. Both were characterized by nervous phenomena; headache, pains in the limbs, psychic depression, sexual frigidity and general asthenia. Wolfsohn and Marcuse found that roentgenoscopy of the sella turcica showed an increase of measurements from normal to abnormal within three

19. Guinon, L., and Reubsæt: Un cas de maladie de Recklinghausen fruste, Soc. pédiat. **9**:263-267 (June 16) 1907.

20. Preiser, S. A., and Davenport, C. B.: Multiple Neurofibromatosis (von Recklinghausen's Disease) and Its Inheritance, Cold Spring Harbor, 1918.

21. Poisson and Lebat: Maladie de Recklinghausen, Gaz. méd.-chir, Nantes, May 3, 1913, p. 357.

22. Feindel, E., and Froussard, P.: Dégénérescence et stigmates mentaux, malformation de l'ectoderme, myoclonie épisodique, acromégalie possible, Rev. neurol. **7**:46-54, 1899.

23. Piollet, P.: Neuro-fibromatose généralisée, Gaz. d. hôp. **75**:1345-1350, 1902.

24. Cushing, H.: The Pituitary Body and Its Disorders, Philadelphia and London, 1912, p. 148.

25. Nicolas, J., and Favre, M.: Acromégalie et maladie de Recklinghausen, Lyon méd. **114**:786, 1910.

26. De Castro, A.: Sur la coexistence de la maladie de Recklinghausen avec l'acromégalie, Nouv. iconog. de la Salpêtrière **25**:41-44, 1912.

27. Wolfsohn, G., and Marcuse, E.: Neurofibromatosis und Akromegalie, Berl. klin. Wchnschr. **49**:1088, 1912.

months' time. Jeanselme²⁸ in an article descriptively entitled "Anomalies of the Sight, the Intelligence, and the Skeleton Associated with Generalized Neurofibromatosis," recorded an accompanying narrowness of the sella turcica. Breton²⁹ (1903), in a case of Addison's syndrome, found at necropsy an enlarged pituitary gland and a sella filled with lymphoid tissue. Spillman³⁰ found a tumor of the sella, and Mossé and Cavalie,³¹ an enlarged and hard hypophysis.

Harbitz (1909) has a valuable article on the allied condition of elephantiasis in connection with generalized neurofibromatosis. He reports a case of a woman, a mongolian imbecile, with an elephantiasis-like growth of the whole thigh and generalized cutaneous tumors. The characteristic mongolian appearance had developed at puberty. Perthes³² (1902) reports a similar case (which Wolfsohn and Marcuse included in the acromegalic cases) and gives the literature of similar conditions. Alexis Thomson's³³ monograph (1900) has a particularly fine illustration of the condition.

Weber (1909) mentions patients with cases accompanied by bony overgrowth of whom the "elephant man" described by Sir Frederick Treves³⁴ is the most extreme example.

A single case of generalized neurofibromas associated with Fröhlich's syndrome, dystrophia adiposogenitalis, is reported by Lier³⁵ (1914) in a boy of 9. Roentgenoscopy showed evidence of a tumor close to the hypophysis.

Thyroid.—Instances of cretinism in patients with Recklinghausen's disease are recorded by Adrian (1903), Strohmeier,³⁶ 1844, and Schuh,³⁷ 1851, 1854 (Adrian, page 461). Schiffner observed true

28. Jeanselme, E.: Anomalies de l'appareil visuel, de l'intelligence et du squelette à sociées à la neurofibromatose généralisée, Bull. et mém. Soc. méd. d. hôp. de Paris **31**:1136-1139, 1915.

29. Breton, A.: La neuro-fibromatose généralisée, Rev. gen. chir. et therap. **17**:17-20, 1903.

30. Spillman: Neurofibromatose et tumeurs cérébrale, Gaz. hebd. de méd. **5**:320, 1900.

31. Mossé, A., and Cavalie: Tumeurs multiples de l'encéphale et de la moelle allongée. Neurofibromatose central, Gaz. hebd. de méd. **2**:789, 1897.

32. Perthes, G.: Ein Fall von Fibroma molluscum, vorwiegend der linken Hand mit Steigerung der Knochenwachsthums, Deutsch. Ztschr. f. Chir. **63**: 103-110, 1902.

33. Thomson, A.: Neuroma and Neurofibromatosis, Edinburgh, 1900.

34. Treves, Sir Frederick: Trans. Path. Soc. London **36**:494, 1885.

35. Lier, W.: Ueber Neurofibromatose, Ztschr. f. klin. Med. **80**:261, 1914.

36. Strohmeier, quoted by Adrian: Centralbl. Grenzgeb. Med. u. Chir. **6**: 461, 1903.

37. Schuh, F.: Ueber die Erkenntnis der Pseudoplasmen, 1851. Pathologie und Therapie der Pseudoplasmen, 1854. Quoted by Adrian, 1903, p. 461.

cretinism in two brothers with the disease (Jullien). Ottolia³⁸ (1908) regarded his case as cretinoid. Debove³⁹ (1905) gives the case history of a man with multiple cutaneous tumors, tumors along the course of the nerves, generalized pigmentation, in connection with thyroid infantilism.

Myxedematous persons are found in the cases of Meige and Feindel, and of Pic and Rebattu.⁴⁰ At necropsy, Bourcy and Laignel-Lavastine found among other glandular lesions, a typical fibrous goiter, with bloody infiltration and diminution of colloid. Muto⁴¹ also found thyroid changes at necropsy. Ehrmann⁴² observed a small thyroid in one case, and the absence of the gland in another. Hallopeau and Ribot⁴³ report typical pigmentation and tumors in a woman in whom exophthalmic goiter was making its appearance. Schlesinger⁴⁴ (1911) saw a case with an associated tetany, the only recorded instance of parathyroid involvement with Recklinghausen's disease.

Suprarenals.—A far from complete review of the literature has disclosed about fifty cases in which a so-called Addisonian syndrome, entirely or partially developed, indicated clinically a suprarenal involvement. Many other cases characterized by these symptoms would doubtless have been found if the reporter's interest had not been entirely taken up by cutaneous and nerve tumors. The author believes that in a great majority of cases of Recklinghausen's disease there will be found certain indications of glandular insufficiencies. A few typical cases showing the clinical picture of Addison's syndrome are detailed:

1. Pic and Rebattu (1907): A man, aged 47; complaint: progressive asthenia; multiple cutaneous molluscous tumors, neurofibromas along the course of the spinal nerves, and widely scattered café-au-lait patches present from birth, together with deep brown punctiform pigmentation of the lower legs; extreme kyphoscoliosis; a myxedematous appearance, caused by infiltra-

38. Ottolia, D.: Considerazioni sopra un caso di morbo di Recklinghausen, *Riforma méd.* **24**:1243-1247, 1908.

39. Debove: Sur un cas de neuro-fibromatose de Recklinghausen, *J. de méd. et de chir. prat.* **76**:566-568, 1905.

40. Pic and Rebattu: Un cas de maladie de Recklinghausen, *Lyon méd.* **108**:636-643, 1907.

41. Muto, A.: Contributo allo studio del morbo di Recklinghausen, *Riv. di patol. nerv.* **15**:656-670, 1910.

42. Ehrmann: Zwei Fälle von Neurofibromatose, *Wien. klin. Wchnschr.* **16**: 139-140.

43. Hallopeau and Ribot, A.: Un cas de maladie de Recklinghausen avec prédominance des troubles pigmentaires et volumineuse tumeur profonde, *Ann. de dermat. et syph.* **3**:613-615, 1902.

44. Schlesinger, H.: Multiple Neurofibroma der peripheren Nerven und der Nervenwurzeln, mit Beinphänomen, *Mitt. d. Gesellsch. f. inn. Med. u. Kinderh.* **10**:124-125, 1911.

tion of the integument down to the shoulders; intellectual faculties formerly intact, weakened. The extreme asthenia was accompanied by hypotension and vasomotor troubles evidenced by Sergent's white adrenal line.

2. Ottolia (1908): A small underdeveloped man, cretinoid; scoliosis and deformation of bones of head; generalized tumors; pigmentation all over the body including the buccal mucous membranes; intellectual inferiority; slowness of movements; obtused and diminished sensibilities.

3. Thiebierge⁴⁵ (1898): A woman, aged 56; pigmented patches small and large, identical with those of neurofibromatosis, over trunk since birth; no tumors, extreme asthenia and gastric troubles for two years; with onset of this condition there occurred generalized discoloration of the skin of the face and body; alteration of character, melancholia, loss of memory.

4. Thiebierge: A man, aged 50; typical tumors and deep brown pigmentation; gastric trouble progressive to death.

5. Jullien⁴⁶ (1910): A woman, aged 43; tumors at 2½ years of age; pigmentation and bronzing of the face at 7; irregular menstruation; at puberty, headaches, gastric distress and vomiting. At present, pigmentation of neck and hands, Addisonian mask, large pigmented patch on mucous membrane on inside of cheek; gastric disorders; lumbo-abdominal pains; quickly fatigued. There was a recurrence in situ of a plexiform neuroma removed from the hypogastrium.

6. Kahn⁴⁷ (1910): A man, aged 42; at the age of 33 pigmentation and multiple tumors occurred; since that time there have been anorexia, vomiting, lumbar pains, exophthalmos, asthenia and pulmonary tuberculosis. Kahn reports this case as one of Addison's disease, but the tumors, the absence of pigmentation on the mucous membranes and the lack of necropsy findings fail to support this diagnosis.

Such is the picture—one of degeneracy and lack of resistance. The exciting causes which bring into activity the underlying tendencies (congenital, hereditary, or familial⁴⁸) in these persons, may be any one of many varying stimuli, such as puberty, pregnancy, the menopause, trauma and infections—such as typhoid fever or tuberculosis—but I believe that the stimulus, whatever it may be, is purely accidental, and that only the inherent tendency is constant.

NECROPSIES IN WHICH THE GLANDS OF INTERNAL SECRETION HAVE BEEN EXAMINED

So far as the writer knows, there have been fourteen necropsies with examination of the ductless glands. Twelve of these were cases

45. Thiebierge, G.: Un cas de maladie de Recklinghausen sans fibromes cutanées ni fibromes nerveux, Soc. méd. hôp. de Paris **15**:143-149, 1898.

46. Jullien, A.: Neurofibromatose généralisée, Thèse, Paris, 1910.

47. Kahn, I. N.: Report of a Case of Molluscum Fibrosum, Addison's Disease and Pulmonary Tuberculosis, New York M. J. **2**:114, 1910.

48. As regards the familial character of Recklinghausen's disease, Preiser and Davenport found that out of 115 children of parents affected with neurofibroma, fifty (43.5 per cent.) were affected with the disease.

in which a more or less complete Addisonian syndrome had been found; two cases lacked such phenomena. In twelve of the cases, or 85 per cent., including the two without Addison's syndrome, involvement of the suprarenals and other glands was found. In two cases, both of which clinically indicated suprarenal involvement, there were only minor histologic changes in the suprarenals.

The proof of glandular dystrophies offered by changes in the glands found at necropsy, even though so large a proportion of the few cases examined were positive, is, nevertheless, interesting rather than convincing; even in undoubted Addison's disease, the suprarenals are occasionally intact at necropsy. Furthermore, as is well known, a general dysfunction of the glandular system may be clinically manifest for a considerable time before any great changes appear in the structure of the glands. No stronger proof of glandular involvement is needed than the clinical conditions shown. However, as the necropsy examinations in question have not formerly been assembled, they are here detailed, together with a case in which a tumor of the suprarenals was found in a living subject afflicted with neurofibromatosis.

Necropsy Examinations.—1. Chauffard⁴⁹ (1896): A man, aged 37; pigmentation, neurofibromatosis; increasing digestive disturbances; death, cachetic marasmus. Necropsy: voluminous adenomatous tumor of cortical origin, involving pancreas, suprarenals and lymphatic ganglions; capsular degeneration. Absence of tuberculous transformation of suprarenals characteristic of Addison's disease.

2. Branca⁵⁰ (1897): A case of Marie's disease; a man, aged 43, alcoholic, had multiple pigmented nevi; molluscos tumors; cachetic; tuberculous; intelligence and memory diminished; speech embarrassed. Necropsy: Kidneys red, hard, small; cysts and adhesive capsule; suprarenal capsule congested; no sympathetic nerve involvement.

3. Marie and Couvelaire⁵¹ (1900): Adult male; disease developed late after freezing hands and feet; progressive asthenia; neurofibrosis, becoming generalized with pigmentation; alterations of sensibility; nervous troubles—apathy, anorexia, etc. Extreme skeletal changes; photographs show appalling progressive kyphosis. Death, extreme asthenia. Necropsy: Osteomalacia; intestinal fibromatosis; pancreas sclerotic; splenic artery extremely sclerosed; spleen hard; suprarenal cortex intact.

4. Bréton (1903): A man, aged 48; complaint, extreme asthenia; five years previously, attack of pain in hands and feet; when pain receded, generalized subcutaneous tumors appeared with pigmentation and nevi; no tumors along nerve trunks; had always been sexually frigid; death, profound marasmus.

49. Chauffard, A.: Dermo-fibromatose pigmentaire (ou neuro-fibromatose généralisée). Mort par adénome des capsules surrénales et du pancréas. Soc. méd. et chir. prat. **76**:566-568, 1905.

50. Branca, A.: Neuro-fibromatose intestinale, Soc. Anat. Par. **72**:166-173, 1897.

51. Marie, P., and Couvelaire, A.: Neuro-fibromatose généralisée, Autopsie. Nouv. iconog. de la Salpêtrière **13**:26-40, 1900.

Necropsy: Suprarenal capsules replaced by two masses of sarcomatous tissue; spleen, kidneys and lymphatic ganglions involved; no tuberculosis. Sella turcica occupied by voluminous lymphoid tissue; pituitary gland size of large bean.

5. Bourcy and Laignel-Lavastine (1905): A woman, aged 58; tumors at 15, increased after marriage; generalized lentigo; molluscum pendulum after menopause; many infections; pains, cramps, fornication, changes in sensibility; asthenia. Death, after five years. Necropsy: Fibrous goiter; changes in suprarenals, spleen and kidneys.

6. Merk⁵² (1905): A man, aged 34 (?); neurofibromatosis and pigmentation; intellect diminished; asthenia. Necropsy: Changes in left suprarenal.

7. Raymond and Alquier⁵³ (1908): A woman, aged 74; cutaneous fibroma; pigmentation; no neuromas; headaches; vertigo; profound asthenia. Necropsy: Suprarenals occupied by generalized sclerosis; at one point that had escaped sclerosis, there was a hyperplastic nodule of spongocytes; kidneys sclerotic. Hypophysis showed alternating layers of sclerosis and hyperfunctionating tissue.

8. Jullien (1910): A man, aged 70; pigmentations and molluscous tumors since birth; augmentation at puberty; extreme asthenia; apoplectic death. Necropsy: Suprarenal capsules voluminous with brown points of epithelial hyperplasia; spleen, voluminous, sclerotic.

9. Muto (1910): A woman, aged 53; gross tumor from infancy; in mature life, generalized eruption of small papules, 3,000 at death. No nervous symptoms. Death, general marasmus. Necropsy: Intense pigmentary infiltration of all the cortical zone of the suprarenals; modification of cervical sympathetic. Histologic changes of pituitary and thyroid.

10. Vignolo-Lutati⁵⁴ (1911): A man, aged 25; pigmentation at birth; skin tumors at puberty. Three years before death, loss of strength, cramps, nausea, vomiting, bronzing of face. Death, cachexia. Necropsy: Sclerosis of the suprarenals.

11. Orzechowski and Nowicki (1912): A girl, aged 18; multiple neurofibromatosis; menstruation never established; intelligence low; troubles of eye and ear. Necropsy: Chromaffin system hyperplastic; pituitary gland only slight abnormalities.

12. Saalman⁵⁵ (1913): A woman, aged 35; typical Recklinghausen's disease. Death from pulmonary embolism after operative removal of elephantiasic tumor from the arm. Necropsy: Hypernephroma, originating in a suprarenal rest, found in liver. Suprarenals normal.

13. Bosquet⁵⁶ (1913): A man, aged 46; cutaneous and nerve tumors; skin a uniform dirty yellow as in Addison's disease; inferior psyche; sexual

52. Merk, L.: Ueber die multiple Neurofibromatose, *Arch. Derm. u. Syph.* **73**:139-145, 1905.

53. Raymond, F., and Alquier, L.: La maladie de Recklinghausen. Ses variétés nosologiques, *L'Encephale* **3**:6-35, 1908.

54. Vignolo-Lutati, C.: Recklinghausenschen Krankheit, *Monatschr. f. prakt. Dermat.* **52**:51-70, 1911.

55. Saalman: Ueber einem Fall von Morbus Recklinghausen, mit Hypernephrome, *Virchows Arch. f. path. Anat.* **211**:424, 1913.

56. Bosquet, T.: Maladie de Recklinghausen et capsules surrénales, *Echo méd. du Nord* **17**:329-332, 1913.

frigidity; anorexia; pains in extremities; profound asthenia. Necropsy: Right suprarenal almost entirely transformed into an epithelial tumor; polymorphic cells; cystic and hemorrhagic formations.

14. Preiser and Davenport (1918): A man, aged 45; after lead poisoning, twelve years previously, generalized tumors and pigmentation; headache; dizziness, palpitations, vomiting, generalized pains. Death, general asthenia. Necropsy: Pigmentation of liver and spleen; slight histologic changes in suprarenal, pituitary and thyroid glands.

15. Kawashima⁵⁷ (1911): Woman in puerperium; multiple cutaneous and nerve tumors; marked kyphoscoliosis. Tumor of suprarenal medulla consisting of atypical hyperplasia of giant multinuclear cells.

TREATMENT BY OPOTHERAPY

This should apparently be a suggestive subject, but the literature contains next to nothing on it. Revilliod,⁵⁸ 1900, in a typical case of Recklinghausen's disease with Addisonian syndrome, controlled the symptoms by use of suprarenal extract. When the extract was discontinued, the asthenia reappeared, and disappeared again when suprarenal extract was again used. Gabriel,⁵⁹ 1911, reported good results in two patients also with the use of suprarenal extract. Preiser and Davenport obtained no results with either thyroid or suprarenal extract in their case in which death occurred from progressive asthenia. One case is reported (Schoonheid⁶⁰) in which ovarian extract was tried without effect.

In diseases of somewhat similar type, adiposis and lipomatosis, Lyon⁶¹ states that thyroid preparations have given better results than any other medication, and that other forms of glandular therapy should also be tried. As is obvious, the glandular field of therapy is practically untouched in Recklinghausen's disease, and should be given a thorough trial, especially as epinephrin, thyroid and pituitary extract have all given good results in the condition of osteomalacia, which so frequently attends the disease.

REPORT OF A CASE

Recklinghausen's Disease with Evidences of Endocrine Dysfunction

History.—A white unmarried girl, aged 20, born in the United States, and having no regular occupation, was admitted, March 8, 1919, to the Skin Clinic of the Beth Israel Hospital, complaining of progressive cutaneous troubles.

57. Kawashima, K.: Ueber einem Fall von multiplen Haut fibromen mit Nebennierengeschwulst. Ein Beitrag zur Kenntnis des sogenannten Morbus Recklinghausen, Virchows Arch. f. path. Anat. **203**:66-74, 1911.

58. Revilliod, H.: De la neurofibromatose généralisée et de ses rapports avec l'insuffisance des capsules surrénales. Thèse, Genève, 1900.

59. Gabriel: Fall von Recklinghausen'scher Krankheit mit Osteomalacie, Berl. klin. Wchnschr. **48**:133-134, 1911.

60. Schoonheid: A Case of Multiple Neurofibromatosis of the Skin, Nederlandsch Tijdschr. v. Geneesk. **2**:1639, 1913.

61. Lyon, I. P.: Adiposis and Lipomatosis, Arch. Int. Med. **6**:28-120, 1910.

Her father and mother were alive and well; her maternal grandparents died of old age; her paternal grandfather, 76 years of age, was well; her paternal grandmother died of a disease the nature of which was unknown; one brother and three sisters were alive and well; another brother was suffering from a nervous breakdown due to recent business troubles. There was no history of miscarriage or of dead brothers or sisters. Syphilis, tuberculosis and cancer were denied.

The patient had had measles in early childhood; she had had no other infectious diseases, but gave a history of constant complaints and suffering from minor ailments. For several years there had been severe drawing frontal headaches; these appeared weekly, lasting for three days, and were worse on rising. During damp and changing weather, there were indefinite pains in the extremities. For the past eight years the vision of the left eye had been gradually decreasing. For three years she had suffered once a fortnight, from attacks of weakness, faintness and precordial pressure of one day's duration. Appetite and digestion were poor; there was no increased frequency of urination, excepting occasionally at night. During the past year, nocturnal restlessness and insomnia had been present. The patient had always had difficulty in learning; she did not progress with her classmates, and was finally compelled to leave school while still in a low grammar grade. She had always had attacks of depression and melancholia.

Menstruation, which began at the age of 14, was regular every four weeks, lasting three days and accompanied by severe bearing down abdominal pains during the first two days; the flow on the first day was profuse, but was scant for the remaining period.

Cutaneous Conditions.—The mother stated that while the patient was but a few months old it was noticed that the right side of her face seemed to grow more rapidly than the left, and that it was of a darker color. This nevoid growth increased in height and extent; it finally spread down the neck to the collar bone. At the age of 4, freckles appeared on the skin of the trunk; these increased rapidly in number and distribution so that the face, neck, trunk and extremities became covered with numerous yellow and brown spots. Round, painful tumors later appeared on the scalp and the lower vertebral region and were excised when the patient was about 8. In 1915, when she was about 16, she was in Mount Sinai Hospital, from March 1 to 15, for the removal of painful tumors of the dorsal and sacral regions. The pathology of these growths was that of neurofibroma. At this period, 1915, the pigmented nevus on the face and neck had become darker in color and was covered with small warty growths and painful soft tumors resembling those of the back and scalp; the latter were also removed. In 1919, two months prior to her admission to the clinic, the painful tumors on the face and neck began to recur.

General Examination.—The patient was short and obese, with mental and physical underactivity. Her movements were slow and clumsy; she answered questions with difficulty; the facial expression was stupid and she never smiled. The head was large; the face, flat and asymmetrical and drawn to one side in talking. The nose was broad; the lips, thick; the right half of the tongue, hypertrophied. The ears were large, and the right auricle was involved by the nevoid lesion of the face and neck. The upper and lower jaws were enlarged; there was a wide space between the two upper central incisors and a small space on each side between the middle and lateral incisors; the canine teeth were small, pyramidal and pointed. The fingers were short and thick and show hyperextensibility.

Examination of the nose, eyes, ears and throat revealed nothing abnormal. The neck was short and fat, and the thyroid gland was of moderate size and soft. The lungs, heart, spleen and liver were apparently normal. The breasts were large and pendulous. The temperature was normal; repeated pulse rate determinations varied between 72 and 80 a minute; the respiratory movements were normal. The blood pressure varied from 106 to 122, systolic, and 60 to 66, diastolic; it was not taken during any of the attacks of faintness, and possibly at these periods it might have been much lower. Stroking the skin produced a mild erythema which disappeared rapidly.

Repeated urinary examinations disclosed nothing abnormal. Chemical examinations of the blood gave these results: blood sugar, 0.07 per cent.; carbon dioxide, 60 per cent.; urea nitrogen, 8 per cent.; nonprotein nitrogen, 30 per cent.; creatinin, 1.2 per cent. The low level of the normal blood sugar finding and the low urea nitrogen content indicate a tendency to a diminished metabolism. The Wassermann reaction, the tuberculosis and the gonorrhea complement-fixation tests of the blood were negative, as was also the radiograph of the skull.



Fig. 1.—Pigmented nevus on face and neck of author's patient.

Dermatologic Examination.—The general cutaneous surface showed the presence of uncountable yellow, café-au-lait and dark brown macules, round, oval and irregular in shape, and varying in size from that of a pin-point to that of a quarter dollar. These were most numerous on the trunk and less in number on the face, neck and extremities. There was no pigmentation of the buccal mucous membranes. There was increased pigmentation, especially at the nipples, the anterior axillary folds and points of pressure. Covering the right half of the neck from the midline in front to the anterior border of the trapezius, there was a dark brown, elevated soft growth, with a surface of pedunculated and nonpedunculated soft, warty papules, ranging from the size of a pinhead to that of a large pea, some of which were tender on pressure. This nevoid growth extended up the cheek over the lower maxillary region and down to the clavicle. An egg-sized pendulous mass, tender to pressure, was situated on the upper posterior portion. From the upper anterior portion depended a large orange-sized, pigmented, soft, tender mass which gave a

larger and lower aspect to the right side of the face than the left. The auricle of the right ear was also disproportionately large, as its lower one-third was hypertrophied, pigmented, thickened and extended into the nevoid growth. A 3 inch linear scar ran parallel to and over the lower maxillary bone.

Situated about the middle of the sternum there was large pea-sized, globular, doughy painless tumor which could be compressed, and imparted to the finger a sensation as if it were growing through a hernial ring in the skin. Nowhere else on the skin was another fibroma of this nature found.



Fig. 2.—Dark brown macules on body and arms of patient.

The hair of the scalp was brownish-black, dry, curly and thick, and extended down the temples almost to the eyebrows. The scalp itself was the site of a seborrheic eczema. In the right parietal region there was a 3-inch round, flat smooth scar devoid of hair, the result of an operation for the removal of a painful growth. The eyebrows were heavy, shaggy and wide, but thinned in the outer one-third. The space between the eyebrows was wide and partially covered with hair. There was a moderate hypertrichosis with the presence of hair on the chin, abdomen and back, while the axillary hairs formed a dense bushy growth. Several linear scars were present in the mid-dorsal and sacral regions where painful tumors had been removed.

Course and Treatment.—This case was presented at the meeting of the Manhattan Dermatological Society, March 11, 1919, with the diagnosis of Recklinghausen's disease. There were some doubts expressed as to the correctness

of the diagnosis, because of the absence of neuromas and fibromas. Dr. Wise, however, agreed with the author that the pigmentation, the nevus and the one fibroma of the chest fully justified the diagnosis. As a matter of fact, in spite of the lack of tumors, this was an outspoken case of Recklinghausen's syndrome, one of the well-known *formes frustes*, but destined, as so many of them are, to develop a fuller cutaneous picture.

The patient was irregular in attendance at the clinic, and indifferent to treatment except to that which would give relief from pain. Organotherapy was attempted but it was impossible to test its value in so unreliable a patient. In April, 1920, she appeared complaining of severe pain in the pendulous masses of the face; this was relieved by large doses of coal-tar analgesics. At this time, there were found about two dozen pedunculated, soft, pigmented fibromas, from pinhead to lentil-size, on the right side of the abdomen. In December, 1920, she returned with a request for the removal of the disfiguring masses of the face. Examination of the skin revealed several new large pea-sized fibromas of the right forearm; the small fibromas of the abdominal skin had disappeared, but several, flat, hardly elevated, soft, purplish, hernial growths were found instead. A plastic operation is to be performed on the face and radium is being applied to the nevoid growth. It is hoped that she may agree to try organotherapy.

Summary.—A report has been made of a case of Recklinghausen's disease showing evidences of pluriglandular dyscrasia, with stigmas of suprarenal and pituitary dysfunction predominating. Beginning early in life, there were indications of suprarenal disorder in the form of cutaneous pigmentations, painful new growths, and physical and mental weakness; the history and the physical findings suggest Addison's disease. The abnormal anatomic markings point to faulty pituitary activity. The thyroid gland and the gonads appear to have played only minor rôles in the production of the picture.

The cutaneous symptom, pigmentation, is generally accepted as depending on a disturbance of the chromaffin system, of which the suprarenals are an important constituent. According to Lyon (page 107), pigmentation has long been considered as symptomatic of insufficiency of the suprarenal (nervous) cortex. It is present in many other conditions besides Recklinghausen's disease, "having known or supposed relations with certain glands of internal secretion, e. g., acromegaly, exophthalmic goiter, myxedema, Dercum's syndrome, adiposity and lipomatosis, . . . arthritis deformans, bronzed diabetes, uterine and ovarian affections, etc." It "suggests a possible relation to the suprarenal glands or to the chromaffin system in general." The fibromas, neurofibromas, plexiform neuromas, and nevi depend for their presence on a congenital or local predisposition and a faulty endocrine-sympathetic system.

It has been shown that the cortex in man constitutes about 90 per cent. of the suprarenal gland, and that in lower animals it is much smaller. The more developed intellectually is the person the more developed is the brain, and the larger is the cortex of the suprarenal glands. It is therefore possible that the mental symptoms in Recklinghausen's disease have some relation to some trouble in the suprarenal cortex.

The following tabulation gives a tentative suggestion of the relationship between the various symptoms of the case to the various endocrines.

Suprarenals: Attacks of weakness, faintness and precordial pressure; hyperesthesia; muscular pains; poor vasomotor tone—diminished skin stroking reaction, low blood pressure; diminished metabolism—low blood sugar and urea nitrogen; anorexia; nocturnal frequency of urination; insomnia; mental

symptoms; abnormal hair growth—hypertrichosis of face, back, axillae, abdomen and between the eyebrows; obesity; dermatologic condition—pigmentation, fibromas, neurofibromas, nevus.

Pituitary: Periodic, frontal headaches; poor vaso motor tone; low blood sugar; nocturnal frequency of urination; insomnia; mental symptoms; low downgrowth of hair of scalp; structural defects—short and obese, shape, size and asymmetry of face and head, prognathism, enlarged right ear, spacing and character of teeth, hyperextensibility of fingers.

Thyroid: Hyperesthesia; poor vasomotor tone; low urea nitrogen; thinned outer one third of eyebrows; obesity.

Gonads: Menstrual symptoms; abnormal hair growth; obesity; dull lethargic mentality.

COMMENT

Ewing,⁶² writing on the origin of fibromas, states that the exact point of origin is still undetermined. That many of them arise from misplaced islands of tissue according to Connheim's theory, is very probable. Other fibromas may depend on local irritation and disturbance of nutrition. In a third group, the clinical features point to a congenital or local predisposition, of which multiple neurofibroma is the best example. It is especially in the second and third etiologic classes that one encounters the less definite tumorlike processes which it is sometimes difficult to classify, and in which one must recognize the cumulative influence of inflammations and chronic disturbance of nutrition and the passage of inflammatory into self-perpetuating neoplastic processes. Recklinghausen showed that the fibroma molluscum arises from the cutaneous nerve filaments. In 1882, he traced degenerating nerve fibers in several characteristic cases and stated that all these tumors arise from nerve trunks or filaments.

"Many authors trace a connection between neurofibroma and many angiofibromas and naevi. They are sometimes associated with xanthoma (Delore, Poncet), and rarely with multiple lipoma (Vallas, Mouchet). Some early lesions suggest an origin from the connective tissue about the sweat-glands, but even here the process has been traced from nerve fibers belonging probably to the sympathetic system." Ewing also asserts that "it is probable that the great majority of actively growing fibromas and fibrosarcomas of the limbs are of neural origin."

"It is generally assumed that the victims of fibromatosis are the subjects of congenital malformation of the ectoderm which under a great variety of exciting causes may slowly or rapidly develop one or more of the manifestations of the disease."

62. Ewing, J.: *Neoplastic Diseases*, New York, 1919, p. 151.

The Italian endocrinologist, Pende,⁶³ has presented a most suggestive theory as to the causation of Recklinghausen's disease—a theory which is particularly interesting in view of the facts set forth in the present article. Pende⁶⁴ (1909) expressed his opinion (with, to quote Muto, "many learned arguments") that the sympathetic nervous system and the glands of internal secretion constitute two physiologically and pathologically synergic systems, so that a morbid process localized in one system makes its effects felt in the other; he maintains that a whole series of affections which have been included either under diseases of the nervous system or in the group of disorders of the glands of internal secretion should be combined into one family group of endocrine-sympathetic dystrophies. The common symptomatic picture would consist essentially of a more or less complex dystrophy (disturbances of metabolism and anomalies in tissue development), accompanied by symptoms due to disturbances in the functioning of one of the endocrine glands. Among such dystrophies, he places scleroderma, chronic dystrophic rheumatism, painful lipomatosis and neurofibromatosis. For the production of these conditions, two factors are required: (1) a constitutional factor represented by an abnormality of the endocrine-sympathetic system, which may be hereditary, intra-uterine, or extra-uterine during the period of growth; and (2) an accidental factor, such as shock, trauma, toxic poison, infection, etc., which through its effects on the endocrine-sympathetic system acts as a stimulus to embryonal elements of the sympathetic system and the skin.

Much the same idea is expressed by Lyon,⁶⁵ who concludes that the various clinical groups of fatty deposit, Dercum's syndrome, the lipomatoses, "adipositas cerebialis," etc., are essentially identical, being only variations of a common morbid process. "They all show a tendency to be characterized by constitutional symptoms of wide variety including especially psychic, sensory, motor, vasomotor, secretory, and trophic manifestations." Special attention is called to various arthralgic and arthritic and neuralgic and neuritic manifestations as belonging to the constitutional symptomatology of the morbid process.

The etiology of the process, thus broadly considered is unknown. Only two views, connecting the process with disturbances of the nervous system or of

63. Pende, N.: Sistema nervoso simpatico e glandole a secrezione interna. *Il Tommasi* **31**: 1909. *Pathologia dell apparecchio surrenale e degli organi parasimpatica*, Soc. Editrice Libreria, 1909. *I nuovi orizzonti della fisiopatologia delle secrezioni interne*, *Med. ital.* **6**:129-132, 153-157, 1910.

64. The translations from Pende are from exact quotations found in Muto's article, *Riv. di patol. nerv.* **15**:656-670, 1910. The original sources were not available.

65. Lyon: *Adiposis and Lipomatosis*, 1910. In this work Lyon makes no specific mention of Recklinghausen's disease, but what he says is equally applicable to this condition, and is quoted here for this reason.

the glands of internal secretion, seem broad enough to harmonize with all the facts. These two views are not necessarily opposed, but can be resolved into one, by assuming that the nervous system is secondarily disturbed by a primary disturbance in the glands of internal secretion, or vice versa. The pathological findings and the general evidence suggest the view that the process is related to alterations in the glands of internal secretion, many writers laying special stress on implication of the pituitary gland in the pathogenesis.

However, the complex mutual relationships between all the glands suggests that one or more or all of them may be concerned in the pathogenesis, and that the variation in symptomatology of the different groups and cases may depend on the varying degrees of involvement of these several glands and the nervous system.

As experimental work tending to show the relationship between the internal secretions and the production of tumors, pigmentation, etc., in conditions such as Recklinghausen's disease is almost prohibitive, it is interesting to note, even though the bearing be remote, the conclusions of Loeb⁶⁶ on the internal secretions as a factor in the origin of tumors in mice. He found that for the development of cancer three factors were necessary: (1) the hereditary, (2) the physical stimulation, irritation, and (3) the chemical stimulation, the internal secretions. The internal secretion seems to cause cancer only in cooperation with hereditary factors. On the other hand, hereditary factors need, at least in some cases, the cooperation of hormones in a definite quantity, if cancer is to develop.

CONCLUSIONS

In view of the previously reported cases, and my observations in other cases as well as in the one here reported, I believe: (1) that Recklinghausen's disease is a complex of cutaneous and general symptoms depending essentially for its etiology on endocrine dysfunction.

(2) That the great majority of cases would show definite signs of endocrine-vegetative disorders, if they were carefully examined for these findings.

(3) That all cases of Recklinghausen's disease tend finally to develop such symptoms, unless there is some compensatory halting of the glandular dystrophy, and that eventually death, unless from intercurrent diseases, will in all probably result from progressive asthenia.

(4) That the term neurofibromatosis should not be used synonymously with Recklinghausen's disease, as neurofibroma or fibroma constitutes only one type of the cutaneous lesions.

(5) Pigmentation is a frequent skin lesion and may be present without any signs of fibromatosis.

66. Loeb, L.: Internal Secretions as a Factor in the Origin of Tumors, *J. M. Res.* **40**:477, 1919.

(6) A syndrome covering a multiplicity of symptoms must be designated by a term broad enough to include them all. At the present time we have no better name than Recklinghausen's disease.⁶⁷

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67. In addition to the references already given, the following cases in which endocrine dysfunction is apparent, may be of interest:

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RADIUM TECHNIC IN THE TREATMENT OF MALIGNANT DISEASES OF THE SKIN

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During the past few years radium has come to occupy an important position in the treatment of malignant diseases of the skin. The literature on this phase of radium work is so abundant that it would seem more important to devote time to a discussion of technic rather than to a further discussion of its merits in this field. With this in mind, I present, in part, at least, the methods employed at the Memorial Hospital. Since it is frequently easier to illustrate a method than to describe it, considerable use has been made of photography in an effort to show the types of lesions found best suited to various forms of application.

Skin lesions are so readily accessible that one of the most serious handicaps in the use of radium for the treatment of malignant diseases is overcome at the outset. The three important factors to be considered are: the selection of proper filtering materials, accurate approximation of the radium to the lesion, and dosage. Of the three, perhaps accuracy of approximation is the most important factor. Skin lesions are so readily accessible that equally good results may be obtained with a wide range of filtration and dosage. If dosage be not entirely overdone at the start, it can be readily supplemented; but, unless the radium is applied accurately to the entire surface in question, failure will result. If one small portion of the lesion be under-treated, or left untreated, the disease will continue, and the result will be credited as a radium failure. We have long since passed the time when a piece of radium may be placed in the neighborhood of a malignant lesion and a favorable result expected.

The relative variations in structure of these lesions are so great that it is impossible to lay down specific rules for filtration in any particular type of growth. The operator must bear in mind the physical properties of radium and their relation to the type of filter at his disposal. He must also visualize the pathologic conditions in the individual case, and then, by judicious correlation of the two, determine the amount of filtration required to affect the tissues well beyond the limits of the growth, with as little actual destruction as possible. It is possible, of course, to destroy any accessible lesion by the use of unfiltered radium alone, but here the effect is largely one of cauterization and is scarcely superior to the old-fashioned escharotics. A reason-

able amount of destruction, confined to an ulcerated area, is in no way detrimental, but a limit must be placed on the amount of gross destruction in the neighborhood of normal tissues. Fortunately, cancer cells have a greater susceptibility to radiation than does normal tissue, so that it is possible to destroy all of the malignant cells within a given area with a minimum of damage to the normal tissues, providing proper methods are used.

At the Memorial Hospital we feel that we are fortunate in being able to use radium emanation exclusively. This in no way alters the procedure or renders it different to that employed by the operator using



Fig. 1.—A case of lupus erythematosus with skin areas partially marked off preparatory to treatment.

the salt itself. It does, however, afford us the advantage of a wide range of usefulness for the radium. It permits of having a large number of tubes of varying strength and of being able to change the emanation tubes from one type of filtering tube or applicator to another without appreciable danger from breakage and loss. It is frequently found advisable to use unfiltered radium emanation and this, of course, can be done without the risk of serious loss from the breakage of a tube, such as would be entailed by an operator using a tube of the salt itself.

FILTERED AND UNFILTERED RADIUM EMANATION

By unfiltered emanation we mean emanation contained in a very fine, thin, glass capillary tube filled and sealed at the ends. Since the alpha rays of radium have a penetrating power of approximately 0.8 mm. of water, it will at once become apparent that the thin wall of the glass tube removes practically all of these rays. The unfiltered tubes may, therefore, be used for the purpose of obtaining an intense beta ray radiation with comparatively little gamma ray effect, since the latter are very much less in amount than the former. The beta rays of radium have a penetrating power equivalent to approximately 3 mm. of water or 250 cm. in air. Water has been selected as a medium for comparison since it bears some relation to the penetration in body tissues. By the interposition of various thicknesses of filtering metal we are able to remove a part or all of the beta rays, and, by increasing the thickness of filters, a large percentage of the gamma rays. By visualizing the pathologic condition to be overcome as far as possible, it is possible to select a filter which will afford the necessary protection



Fig. 2.—Two types of wooden applicators with the unfiltered radium emanation tubes held in place by paraffin.

against the softer rays and still permit the passage of a sufficient quantity of more penetrating rays to radiate thoroughly the area in question. While in our physical laboratory a large number of metals have been studied experimentally, in the practical side of the work we have found it advantageous to confine ourselves to a few metals of various thicknesses as filters. For example, 0.2 mm. of aluminum removes approximately 25 per cent. of all radiation. This means that most of the softer beta rays are removed, but only a negligible quantity of gamma rays. Aluminum is an excellent material to use when such a light filter is required, but for greater filtration it is more practical to use a heavier metal, thereby obviating the necessity for increasing the thickness to a considerable extent. The filter which we employ more frequently than any other in the treatment of skin lesions is 0.5 mm. of silver. This removes about 95 per cent. of all radiation. Practically all of the beta rays are cut out, but we have left a wide range of gamma radiation. By increasing the filter to 1 mm. of platinum, 97 per cent. of all radiation is excluded. Apparently this variation of 2 per cent. amounts to little, but if we consider the fact that the therapeutic rays

are those which penetrate the filter, it will readily be seen that there is considerable difference between the half millimeter of silver and the millimeter of platinum. With the former, 5 per cent. of the total radiation reaches the tissue, whereas with the latter only 3 per cent. is available, which permits the use of a much heavier and more penetrating dose in comparison to the superficial absorption produced. The variations between 0.5 and 1 mm. of platinum and between 1 and 2 mm. of platinum are so slight that they need not be considered from the standpoint of dermatologic work. The only radiation we employ which is



Fig. 3.—The applicators illustrated in Figure 2 in place.

unfiltered, in the strictest sense of the term, is an active deposit of radium prepared by exposing a thin piece of lead foil to the emanation under pressure for a period of time sufficient to permit as large an amount of deposit as the concentration will afford. This product is unstable in that it deteriorates rapidly, but it affords a means of radiating a surface intensely, if necessary, without any appreciable deeper penetration. We have found certain uses for it which will be described later.

To summarize: We use for practical purposes in our every-day work, in addition to this last mentioned active deposit, the so-called unfiltered or bare tube, which permits us to utilize practically all of the

beta and gamma radiations: a tube of 0.2 mm. of aluminum, which removes only the softer beta rays and a few of the gamma rays; a 0.5 mm. silver tube which removes nearly all of the beta rays and an appreciable percentage of the softer gamma rays; and a millimeter of platinum which removes all of the beta rays and a large percentage of the softer gamma rays. I have not entered into a discussion of many of the other filters in common use, such as lead and brass, although they are fully as good when used in proper thicknesses. We have used the aluminum because in a thickness for practical use it affords slight filtration. Silver, which as I stated we use most, machines readily, is easily cleaned, and the tube can be easily enameled in various



Fig. 4.—Lead foil both cut and uncut and prepared for application to the under surface of the lid.

colors, so that one tube may be distinguished from another. The platinum we have found to be the most practical heavy metal for all-round purposes. With these types of filter we have found it possible to handle the skin work satisfactorily, and consequently we have not considered it advisable to complicate matters by the use of a wider range of either metals or thicknesses of metals.

DOSAGE

As for dosage, it would be almost impossible and totally impracticable to set down any fixed rules of value for individual operators. During the past year, experimental work in our physical laboratory,

under the direction of Mr. Failla, has been directed to this end, and while we hope soon to be able to place dosage on a much more scientific basis than heretofore it is still too early, as well as outside its sphere, to make, in this paper, a report on it. In the earlier part of our work



Fig. 5.—Placing of prepared lead foil, having active deposit of radium on its inner surface, beneath the eyelid.

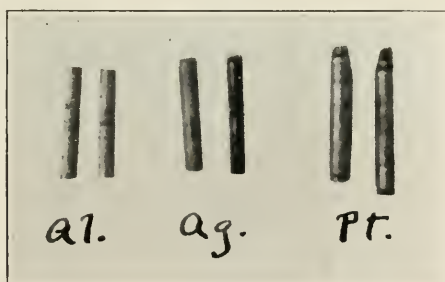


Fig. 6.—Sizes of aluminum, enameled silver and platinum tubes used as filters in dermatologic work.

we arrived at certain empiric doses after long, and in many instances painful, experience, and I daresay this experience has been shared by many other workers. The wide range of filters used by operators in

various clinics makes it doubly hard to arrive at a uniform dosage table for certain types of lesions, and the individual lesion presents so many variations that the task would be well nigh impossible. In general, however, when the filter has been determined on, the dose should be a massive one: that is, a quantity of radiation which will produce a noticeable erythema or even a suggestion of superficial destruction. Since silver has been our most common filter in skin work, we have arrived at an empiric unit of dosage with it, estimating it according to the extent of surface involved. With a filtration of 0.5 mm. of silver placed at a distance of 3 mm. from the surface, a unit dosage of 60



Fig. 7.—Placing tubes in position by embedding them in plastic dental modeling compound.

millicurie hours per square centimeter of surface has been our standard. If the lesion is small, that is, only 1 or 2 sq. cm. in extent, this may be increased to 70 or 75 millicurie hours per square centimeter, whereas if it is much larger, the dose will necessarily have to be reduced below 60 millicurie hours per square centimeter on account of the cross-firing. Several other factors must also be taken into consideration in determining the variations in this empiric dosage, such as the unevenness or curvature of the surface, the type of lesion being treated or the proximity of various vital structures.

While it is of great importance to select a proper filter and consequently a proper dosage, it is of still greater importance to obtain accurate approximation of the radium to the lesion. Radiation at a distance is, of course, more uniform because the rays tend to become more homonomous the greater the distance from the surface to be treated, but this is a method of value in only a small percentage of skin lesions, to say nothing of the expense in wasted radiation. In other words, it is in most instances purely a gunshot procedure.

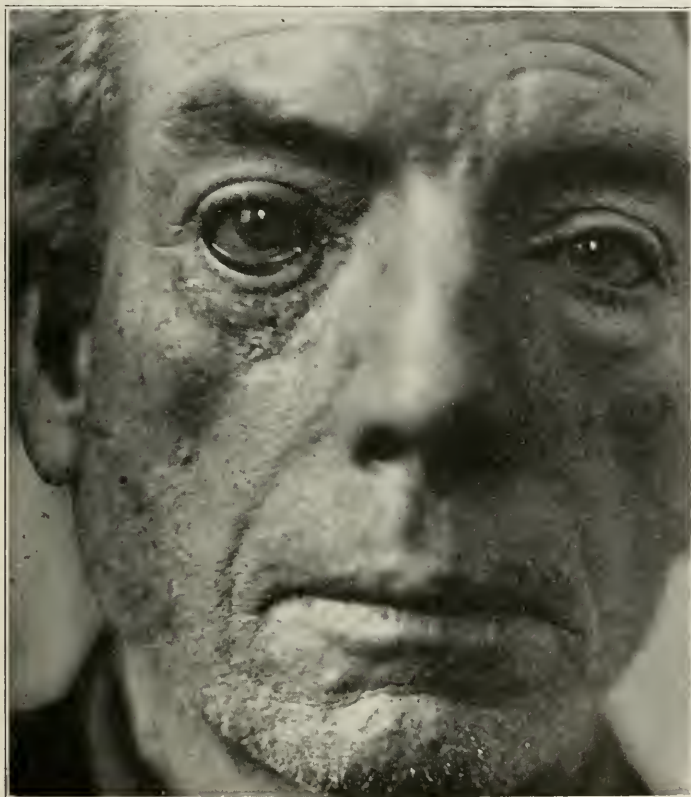


Fig. 8.—Type of small lesion suitable for applying filtered tubes directly on plastic dental modeling compound, allowing it to harden in place, thereby holding the tubes completely in apposition to the lesion.

Accuracy of approximation of the radium to the surface will always give best results with least expenditure of radium, and consequently our efforts should be concentrated in this direction.

VARIETIES OF SKIN ERUPTIONS TREATED WITH RADIUM

In order to illustrate to best advantage the methods of application used, it may be well to discuss certain groups of cases more frequently encountered, indicating the type of applicator used, adding,

if necessary, a few words relative to the filtration and dosage. Our work has been confined almost entirely to the treatment of malignant lesions of the skin, although two or three common and allied conditions have come to our attention so frequently, and have given such good results from the use of radium, that we feel it advisable to include them at this time.



Fig. 9.—Another type of lesion suitable for the same treatment as the lesion in Figure 8.

Lupus of the Skin.—This is a disease that we have been called on to treat rather frequently, and while I doubt if radium is as valuable in this condition as the Finsen light, the results have been fairly satisfactory. The lesion heals with a slight amount of scarring, and only in a small percentage of cases is there a tendency to recurrence. Since the disease is superficial, we have found unfiltered radium the best agent to use in its treatment. Figure 1 shows the skin prepared for the application of radium and indicates the type of applicator used. Radium emanation tubes of equal strength are placed evenly over the

surface of a small wooden block 5 mm. in thickness, and over these tubes a small bit of hot paraffin is poured, which, when cool, holds them readily in place. In case the radium is to be held in place by the hand of the patient or operator, two ordinary wooden tongue depressors may be placed together, held by adhesive plaster and the radium tubes arranged at one end. This affords a handle by means of which the operator or patient may safely hold the radium against the area to be treated. While the 5 mm. of wood remove a small percentage of the



Fig. 10.—Type of lesion requiring protection of the surrounding skin area.

softer beta rays, the chief object is to lend distance to the application. In this way a much more even distribution of the radium is obtained. The area to be treated is blocked off in squares with ink, the squares being slightly larger than the applicator so that there will be no overlapping of the radiation and consequent burning. The applicator may be changed from one of these squares to another after a sufficient dosage has been given. Using this technic, a dosage of 10 to 16 millicurie hours per square centimeter, depending on such varying factors as the

age of the patient and type of skin, has usually been found sufficient to clear up the disease with one application. Figure 3 shows the two types of applicator in place, the one being held by a piece of adhesive plaster and the other by the patient. The former method is advisable unless the areas to be treated are isolated and far apart and the patient very intelligent.

Vernal Catarrh.—This is another nonmalignant condition in the treatment of which unfiltered radium has proved very satisfactory. A small block with unfiltered radium on the surface, as previously illustrated, may be placed over each lid in two areas, so that an efficient radiation is afforded the entire lid. Providing a strong dose of radium is used in this applicator, it need only stay in place a few minutes so that the discomfort to the patient is slight. From the standpoint of

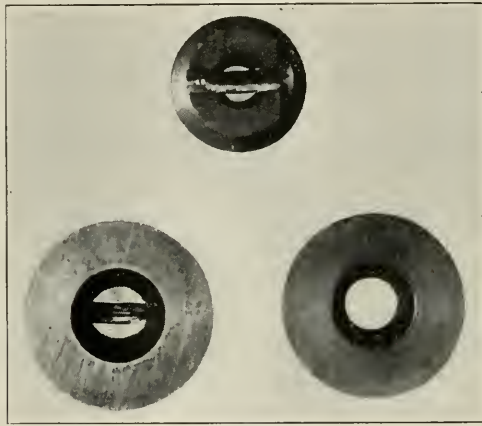


Fig. 11.—Steel cone, with enameled silver tubes, which affords the kind of protection that the type of lesion in Figure 10 requires.

the operator, this method of treatment is preferable because of the slight amount of exposure necessitated. It is not, however, the most efficient and accurate method of applying radium in these cases. The active deposit of radium on lead foil, previously mentioned, is the ideal form in which to apply radium to the under surfaces of the eyelid. Lead foil, 0.1 mm. in thickness, is used on which to collect this active deposit. After the deposit has been collected on the lead foil, the radio-activity may be measured by the same method of ionization as is used in determining the strength of our emanation tubes, and, knowing the total surface area of this piece of lead foil, we may then calculate the strength per square centimeter. The foil is then folded double so that the two surfaces covered by active deposit are in contact. This, of course, doubles the strength per square centimeter. The

folding over is done for the purpose of affording a filtration of 0.1 mm. of lead, that is, the thickness of the lead foil, for protection of the cornea. A piece of this, the size and shape of the lesion to be treated, can then be readily cut with scissors. The eye is cocainized and petrolatum placed beneath the lid; then, with a forceps this small piece of lead foil, the inner surfaces of which are covered by the active deposit of radium, is inserted under the lid in apposition to the diseased area of mucous membrane. We always aim to have the concentration of such a degree that an applicator is required to stay in position only



Fig. 12.—Type of lesion suitable for the use of an applicator made of the dental modeling compound, before and after treatment.

a few minutes. This method is entirely painless for the patient, affords a means of accurate approximation of radium to the parts to be treated, and gives the intense local effect to be desired. The only difficulty about the use of radium in this manner is the exposure of the operator. While the active deposit decays rapidly, it is, nevertheless, very intense in its effect for a short period, and since it is entirely unfiltered the operator must be careful to keep as far from it as possible. The use of long forceps and long handled scissors, especially if many patients are to be treated in this manner, is essential to the safety of the operator.

Figure 4 shows the lead foil used, as well as two small pieces folded and cut ready for use. Figure 5 shows the operator in the act of inserting one of these small pieces beneath the patient's eyelid. In many cases one application is sufficient, although in some of the more obstinate cases two, three or even four applications may be necessary.

Nevi.—In the treatment of nevi, or capillary angiomas, the same method of applying active deposit of radium on lead foil is the ideal technic but, except in special cases, it is to be avoided because of the amount of exposure to the operator necessitated in its preparation. Unfiltered radium on wood, as previously described, is very efficient in the treatment of most of these lesions.

Small Lesions.—For the treatment of many small lesions, such as moles, papillomas or rodent ulcers, one or two small tubes of radium



Fig. 13.—Applicator made for the patient in Figure 12. The illustration at the right shows the applicator ready to be sent to the laboratory; the one at the left shows the silver tubes held in place by paraffin and ready to apply over the lesion.

emanation are required. In Figure 6 these tubes in aluminum, silver and platinum are shown. The selection of the tube and filter depends on the amount of penetration desired. For holding these tubes accurately in place, on such small lesions, we have found the ordinary red dental modeling compound used by dentists in the making of impressions of inestimable value. In Figure 7 the method of using this is illustrated. This modeling wax, when placed in hot water for a few minutes, readily softens so that it is very soft and pliable. A small piece of it is placed over the lesion, and the tubes pressed into place while it is still soft. In a few minutes it hardens in place and adheres to the skin sufficiently to prevent falling off. As a further precaution, in some locations, a small piece of adhesive plaster may be applied over the surface and attached to the skin at either side. It has the advantage of keeping the tubes exactly where they are placed, and

prevents the movement which so often occurs if a small gauze pad is used. It frequently happens in these cases that the movement of a tube 3 or 4 mm. from the original area results in failure to obtain the desired result. Figures 8 and 9 show two patients with cases which we consider suitable for the use of this simple technic. We feel that it is vitally important to simplify the technic in all of these cases as much as possible in order to cut down the amount of exposure to the operator, and thereby safeguard the hands of the various persons called on to handle the radium.

It is sometimes necessary to treat a lesion in a location in which the surrounding parts should be protected from the radiation, for



Fig. 14.—Case suitable for the use of buried radium emanation in combination with a surface application of filtered emanation held in place by the dental modeling compound. The photograph at the right shows the result of this combination of treatment.

instance, a small growth on the scalp. For this purpose Dr. Duane of the Huntington Memorial Hospital, Boston, devised a steel cone, illustrated in Figure 10, and introduced it in our laboratory. This consists of a steel cone with a flat base, having in its top a groove, or several grooves, to hold the filtered tubes of radium. These cones are of various types so that the radium may be placed at various distances; they are made with varying diameters in the central free space. The tubes are readily held in place in the grooves at the top by a drop of paraffin or a small piece of adhesive plaster. The fixed

walls of the steel cone cut out all appreciable radiation extending laterally and permit only treatment of an area covered by the opening in its base. The only disadvantage of such an applicator is its weight.

In Figure 11 is shown a small papilloma of the scalp suitable for such a method of application. The applicator is held in place by the patient, although it may quite as well be strapped there by adhesive tape. At the right the same case after treatment shows that there has been no unnecessary epilation of hair.

Treatment of More Extensive Lesions.—When we treat some of the more extensive and irregular lesions, such as the rodent ulcer illustrated in Figure 12, we must be more careful in our radium distribution. Success or failure will depend almost entirely on the accuracy of the approximation of radium to the involved area. In such cases we make extensive use of the dental modeling compound previously mentioned. After this wax is made plastic by immersion in hot water for a few minutes it is molded over the lesion to be treated

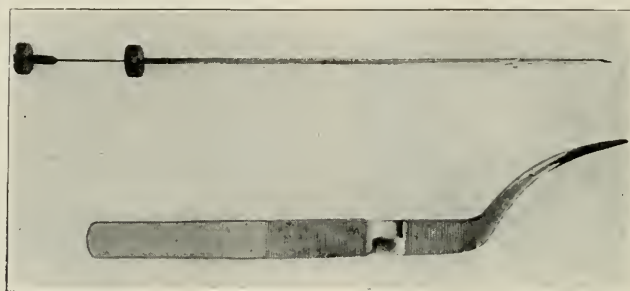


Fig. 15.—Trocar needle used for inserting the fine radium emanation tubes interstitially; below, a special type of forceps found valuable in loading the emanation tubes into the ends of the trocar needles.

and left in place to harden. It is then removed and the area to be treated marked on the applicator in ink. This applicator is then taken to the laboratory and grooves made in it with a small chisel or a heated rod so that the enameled silver tubes may be laid in the grooves at a distance of approximately 3 mm. from the surface. The tubes are so arranged that there is one tube for each square centimeter of surface, and they must also be of equal strength, unless at certain points a slightly stronger dose is indicated, in which case such instructions should be marked on the applicator at the time of sending to the laboratory. When these tubes have been placed in position in the grooves they are sealed in place by pouring hot paraffin over the surface. In addition to holding them in place, this paraffin affords a sufficient filter to remove the small amount of secondary radiation from the silver tubes. I mention silver tubes because we almost

invariably use 0.5 mm. silver as our filter in the treatment of this type of lesion. The applicator is now ready for applying to the growth. It will fit exactly, as the mold has been originally made so that there is no danger of applying the radium at the wrong point. The unevenness of its surface, corresponding to the irregularities of the part, prevents slipping, and it can be readily strapped in place with adhesive tape. Our dosage varies, as I stated before, from 50 to 60 or 65 mc. hrs. per square centimeter of surface, depending on the type of lesion and the amount of cross-firing encountered. Figure 13 shows one of these applicators hardened and marked with ink, ready to have the tubes inserted; the illustration to the left shows it with the tubes inserted and ready for application to the lesion. This particular applicator was made for use on the lesion illustrated before and after treatment in Figure 12.

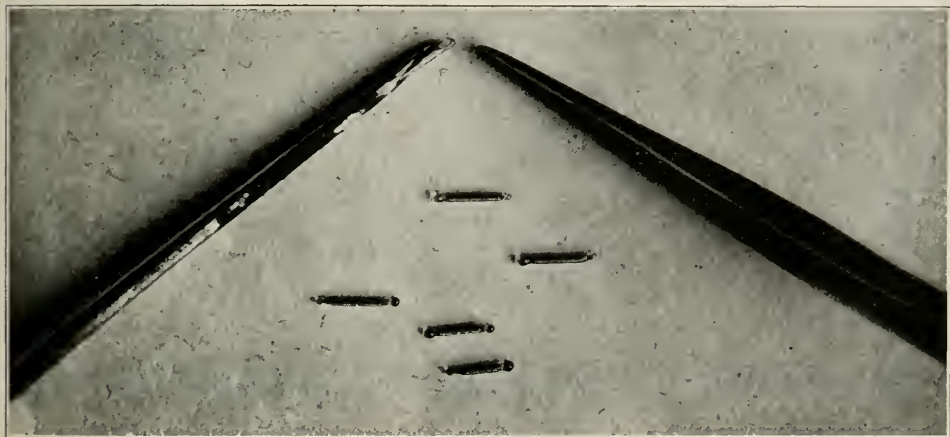


Fig. 16.—Small glass radium emanation tube magnified about five times; also the act of loading one of them into the end of the needle.

We frequently have bulky growths, such as the squamous cell carcinoma illustrated before and after treatment in Figure 14, in which surface applications of radium are inadequate to control the disease. Radium applied on the surface of such a lesion exerts the intensity of its effect on the least important portion of the growth. The superficial part absorbs most of the radiation, even though heavy filtration is employed, leaving the base little affected.

In the treatment of these we have made valuable use of a method which we employ extensively in many of the deeper lesions in other parts of the body, that is, the burying of radium emanation in the substance of the growth. For this purpose we use small glass capillary tubes of radium emanation, similar to those previously described, but

made much smaller in size. They are approximately 3 mm. in length and 0.3 mm. in diameter, and in strength vary from 0.5 to 3 mc. of radium emanation although about 1 mc. seems to be nearer the ideal strength for most purposes.

These tubes are readily sterilized by boiling and are then inserted into the substance of the tumor by means of fine trocar needles. In this manner weak tubes may be distributed uniformly throughout the deeper portions of the growth, thus giving an intense beta and gamma ray effect in the more inaccessible parts of the growth, while a surface



Fig. 17.—A recurrent squamous cell carcinoma of the skin with the skin now intact and the recurrence in the deeper tissues attached to the periosteum over the jaw bone. This case is suited for the combined use of radium emanation and surface application of filtered radium at a distance to afford a very penetrating external dosage without damage to the skin.

application of filtered radium, such as I have previously described, may be used over the entire surface. This method of burying radium emanation has been of inestimable value in reaching portions of the growth which cannot be successfully treated from the surface. It is also a most economical method of using radium since it is placed within the growth so that radiation in all directions is absorbed, and full benefit is derived from both beta and gamma rays.

Figure 14 illustrates a case admirably adapted to this combination of treatment. Figure 15 shows the trocar needle employed in burying the tubes and likewise shows the forceps which we have found to be very useful in placing the tubes in the ends of the needles. Figure 16 is a magnified illustration of the emanation tubes and the act of placing one of these tubes within the end of the trocar needle. This same method may be followed in part by those who have not radium emanation at their disposal but have, instead, the small metal needles with varying quantities of radium salt in their ends. The difference



Fig. 18.—Type of heavily filtered containers, termed "tray" and "pack," used for applying large doses of radium at various distances from the skin surface in order to obtain a maximum of penetration with a minimum of skin absorption. The "danger" label is applied so that there will be no possibility of applying these large doses of radium upside down and thereby causing serious injury to the patient.

is that the metal needle cuts out a very appreciable part of the beta ray activity and, of course, the length of exposure must be very much shorter. We feel that there is considerable advantage in the application of very small amounts of radium in this way, effective over a period of several days or even a few weeks, which makes the method superior to the use of metal needles containing the salt inserted for a few hours and then withdrawn. We have had no trouble from placing a foreign body in this way within the tissues. In the case of an ulcerated lesion

many of these fine tubes slough out as healing progresses, whereas in the solid tumors they become surrounded by a small fibrous capsule and remain harmless.

This method of burying radium emanation tubes is of value in a variety of lesions coming under the care of the dermatologist. Cavernous angiomas respond favorably to their use with a minimum of resultant scar, although several months is required in which to obtain a satisfactory regression. The metastatic cutaneous nodules of melanoma may be dissipated by burying a tube at the base although this in no way precludes the appearance of other nodules. For the individual nodules, however, we have found it to be the method of choice.

Another type of growth, well adapted for the use of these buried emanation tubes, is illustrated in Figure 17. This was a case of recurrent squamous cell carcinoma of the skin with the skin entirely healed but with a deep bulky recurrence adherent to the periosteum over the jaw bone. To supplement the use of the buried tubes with a contact surface application of silver filtered radium, such as that previously illustrated by the dental modeling compound mold, would be inadvisable because of the danger of skin destruction, providing an adequate dosage was given. In cases such as these we take advantage of a heavier filtration, such as 2 mm. of lead or brass, and place it at a distance of from 1 to 3 or 4 cm. from the skin, in order to get a more diffuse or homogeneous radiation. Figure 18 shows two types of applicator which we have found well suited for this purpose. The circular applicator illustrates what we term a "tray." It is simply a small tray made of 2 mm. of lead or brass and of varied shapes and sizes to meet the special requirements of individual cases. In this may be placed any quantity of tubes available and on top of them a lid made of the same material and thickness as the tray for protection in the opposite direction.

The larger applicator, which we term a "pack," is constructed on the same principle as the tray but is much larger. These range in size from 50 to 70 sq. cm. surface area. The bottom is covered by lead or brass, as before, and the notches illustrated are for the purpose of holding tubes placed inside. These tubes are, of course, of varying strength, and so by a rough mathematical calculation the tubes may be so grouped, over the bottom of the pack, that the radiation will be practically uniform throughout. When the lid has been placed in position a "danger" label is always placed on the top for safety to indicate to the one who applies it the top and bottom of the pack or tray. In the use of these heavily filtered applicators we are coming to the opinion that, for most purposes at least, 2 mm. of lead is more filtration than is ordinarily required, and that a corresponding thick-

ness of brass will give us the desired result without removing as many of the therapeutic rays. This we feel will result in a considerable saving of the radium.

In conclusion, I wish to state that most of the methods and applicators herein described are due to the work and ingenuity of the late Dr. H. H. Janeway, the former head of the radium department, and to him we owe the credit for advancing the work in this field to its present status.

A CLINICAL, HISTOLOGIC AND BACTERIOLOGIC STUDY OF A CASE OF MULTIPLE BENIGN SARCOID OF BOECK-DARIER-ROUSSY

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A large number of cases of multiple benign sarcoid of Boeck and Darier-Roussy have been studied at length, chiefly as regards the etiology of the condition, and, as yet, no conclusions have been accepted. In the literature there are about sixty reported cases, and these have been well summarized repeatedly. The author is aware of six unreported cases, so it is impossible to know how many have been recognized. The histologic picture is practically unique, and because it so closely resembles that of a noncaseating tuberculous process, the greatest amount of effort has been directed toward isolation of the tubercle bacillus. A bibliography of the pertinent literature is appended to this article. It will suffice to say here that it is generally conceded that the Spiegler-Fendt type, which resembles the neoplastic lymphodermas, does not belong to the sarcoid group, and that it is questionable whether there is a distinct nodular variety of sarcoid of the extremities which is anything other than either an atypical or a true erythema induratum of Bazin, many of these supposed sarcoid cases having gone on to ulceration, a characteristic foreign to unquestionable sarcoid lesions. In many of the latter alone, tuberculosis has been positively demonstrated. This leaves only the Boeck type of multiple benign sarcoid, or miliary lupoid as it is sometimes called, and the subcutaneous sarcoid of Darier-Roussy as representatives of the group. The Boeck and Darier-Roussy types sometimes overlap in both gross and microscopic characteristics.

REPORT OF A CASE

History.—An Italian woman, 25 years of age, was born in America and married at the age of 18 years. She was the mother of three children, all well, and she had had no miscarriages. Except for measles and "worms" as a child and a history of frequent "colds," she had always been vigorous and well. There was no family history of tuberculosis or of any other disease of special interest. She had always worked strenuously, her labor having been confined mostly to her home. There was no noteworthy menstrual or venereal history.

Eight years ago the patient thought she sprained her left little finger, which was painful and treated for a sprain. About one month later the pain stopped, and this finger became more swollen on the flexor surface in the region of the first and second phalanges and on the extensor surface of its distal phalangeal joint. Gradually these swellings had increased in size and

number on all of the fingers and on the back of both hands and wrists. Similar involvement of the feet and ankles made its appearance about one year after the beginning of the activity of the hands, and it, too, has been slowly progressive. The first lesions occurring on the feet were slightly painful and tender for about one week when first noticed. About two years after the beginning of the hand involvement, the lesions on the face and arms appeared simultaneously as soft red macules which gradually became larger by peripheral extension and coalescence, deeper red, more elevated, and more easily palpable. The majority of these formed within a year.

Physical Examination.—The patient was about 5 feet, 2 inches in height, apparently about five years older than the age given, well nourished and slightly pale. (For description of the skin, see addendum.) There were no gross noteworthy changes of the scalp, eyes, ears and nose, except as mentioned elsewhere. The teeth, except for one carious molar and a slight pyorrhea of the lower gum in front, were in good condition. The tongue was grossly normal. The tonsils were small, with clean crypts, and the pillars and soft palate were a normal red. The pharynx was slightly injected, and there was a slight chronic hyperplasia of the posterior wall of the lymphoid tissue. There was no other gross change of the mucous membrane of the oral or nasal cavities. The cervical lymph glands were not palpable. The thyroid gland was not enlarged, and there were no abnormal pulsations of the blood vessels of the neck. The chest was well developed and of normal symmetry. There was no retraction of the fossae of the base of the neck with deep inspiration, and the excursion of both the lower and apical lung borders was everywhere liberal. No noteworthy findings were elicited in the lungs by inspection, palpation, percussion or auscultation. The heart borders were well within normal boundaries, and the heart tones were clear and unchanged. The lower half of the abdomen in front was somewhat pendulous, and its skin was unchanged except for a few striae gravidarum. The subcutaneous fat of the trunk in front was thick, making palpation difficult. The costal angle was an acute angle. The spleen, liver and kidneys were not palpable, and there were no liquid or tumor masses or evidences of hernia in the abdomen. Splenic dullness was within normal limits. Rigidity and areas of tenderness of the abdomen were absent. The inguinal glands were of normal size. The genitalia were not examined at this time. There was no axillary or epitrochlear adenopathy. The finger and toe nails were unchanged. Sensation was generally normal to touch, heat and cold, and there was no alteration of the superficial or deep reflexes.

There was a bluish-red, sharply defined, soft nodular patch of the right cheek, the center of its medial margin 2 cm. from the angle of the mouth. The lesion was approximately round, and its borders sloped gradually to fade into the color and texture of the surrounding grossly normal tissue. The elevation of the lesion was about 2 mm., and its greatest transverse diameter was 3.5 cm. The skin over it was soft and dry, and there were many dilated blood vessels at its periphery which, in most instances, coursed toward the center. Near the center of the lesion, beneath the superficial layers of the epidermis, were soft, cream colored or light brown, pinhead-sized puncta, composed, apparently, of sebaceous material. The redness faded to light brown with pressure. There were three fused patches of the left cheek similar in all essentials to the one just described, the largest being of approximately the same size and locality as the lesion of the right cheek. A less sharply defined plaque of the same color extended across the nose, only the portion near the

tip on the left side being distinctly nodular. There was considerable dry scaling of the patch on the nose. Pinhead to match-head sized, red and pink, soft papules, rather indistinct, thickly mottled the chin and upper lip. Each of the large, dark red, soft nodular areas described was studded with match-head sized, brownish, firmer nodules, most clearly defined by the aid of the diascope. There were about twenty pinhead to match-head sized, soft and firm nodular lesions of the neck behind the ears near the scalp hairline and as many of the forehead. These varied in color from that of the normal skin to pink or light red. There was an area of the skin over the manubrium a little greater in size than the diameter of a silver dollar, composed of three or four fused deep nodular patches, each a little less than the diameter of a small fingernail



Fig. 1.—A lobe from the finger magnified 60 diameters, showing its division into lobules.

and more distinct by palpation than by inspection, the skin here being but slightly elevated and pink to blue-red.

Deep-seated, blue-red to brownish, nodular patches, chiefly of the extensor surfaces, extended down each upper extremity from the upper scapular region. These patches tended to coalesce to form gyrate arrangements on their respective extremity. The patches were decidedly deepseated and nodular, and this could only be elicited accurately by palpation. The flexor surfaces were relatively free, as was the back of the lower half of the left forearm. The patches were all attached to the skin above and were freely movable over the underlying, deeper subcutaneous tissue.

The hands were lumpy and swollen to the extent of considerable deformity. Several deep, circumscribed, slightly movable, flat, soft and firm nodules, bean to almond size, were present on the back of the hands, about the wrists, and on some or all of the surface of all of the fingers. Their overlying skin was tense and of approximately normal color. The dorsum of the distal phalangeal joint of the index, ring and little finger of each hand was broken down at the present time and covered with a bloody crust, a condition which healed in the course of two or three weeks only to recur in the course of two or three months. The distal phalanges were, in nearly every instance, fixed in partial flexion and some of them were distorted to one side or the other.

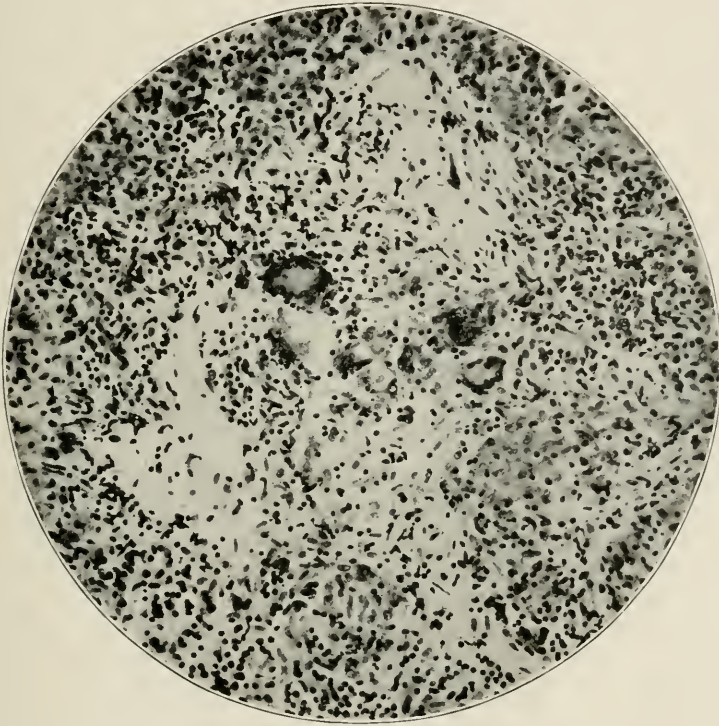


Fig. 2.—Section from the face magnified 130 diameters, showing what resembles a noncaseating miliary tubercle.

There were five painless, soft, globular swellings in the vicinity of the left ankle, chiefly of the outer side, each of about walnut size, deep-seated, and fairly sharply circumscribed, the skin over them being grossly of normal appearance. Also on this side, midway between the back of the heel and the root of the small toe, its lower margin extending to the plantar surface, was a swelling in all essentials similar except that it was blue-red and more firm. There was a swelling of the back of the right heel in the region of the attachment of the Achilles tendon similar to the first swellings of the left foot, except that it was much harder. The lateral surface of this ankle was rather puffy, but there were no circumscribed or definite infiltrations.

Laboratory Examination.—The following findings are in each instance an average of repeated examination:

Blood: The blood findings were: erythrocytes 4,250,000, leukocytes 11,400. The differential leukocyte count was: polymorphonuclear neutrophils, 54 per cent.; large lymphocytes, 18 per cent.; small lymphocytes, 16 per cent.; large mononuclears, 2 per cent.; transitionals, 2 per cent.; eosinophils, 7 per cent.; myelocytic neutrophils, 2 per cent. The percentage of hemoglobin was 75; the color index 0.89. The blood pressure was: systolic, 128; diastolic, 84. Blood cultures were negative. **Blood Chemistry:** urea, 180 mg. per liter; chlorids, 5.09 gm. per liter of plasma; plasma bicarbonate, 49.7 c.c.; nonprotein nitrogen, 26.6 gm. per liter; uric acid, 1.8 mg. per 100 c.c. Body temperature ranged from 96.8 F. to 98.4 F. in the course of twenty-four hours.

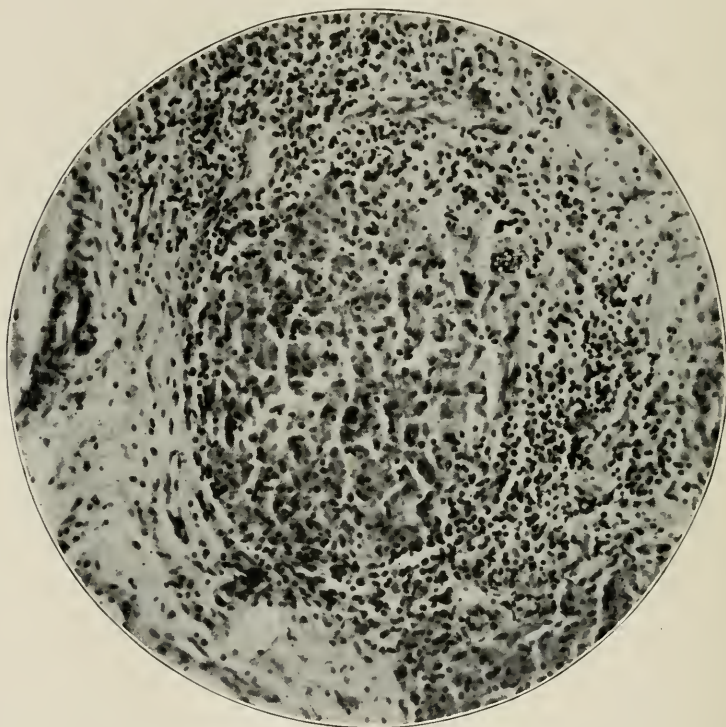


Fig. 3.—Section from the face magnified 130 diameters, showing epithelioid-cell proliferation surrounded by plasma cell connective tissue cell infiltrate.

Urine: The specific gravity was .1017; the reaction, acid; albumin, sugar, acetone, diacetic acid, chemical blood, bile, indican, melanin and Bence-Jones protein were negative. The diazo reaction was negative. Microscopic examination revealed no casts or blood, very few leukocytes, many epithelial cells and a few uric acid crystals. Urine cultures were negative except for contaminating organisms. No tubercle bacilli were found after six hours of centrifugalization.

Sputum and Nasal Secretion: Carefully selected specimens were negative for tubercle bacilli.

Stools: The color and consistence were normal and no tubercle bacilli were isolated. All contained fat (sudan III), starch (Lugol's solution), a few muscle and connective tissue fibers and grossly visible undigested food.

Wassermann Reaction: This was negative to five different antigens.

The von Pirquet test was negative.

Tuberculin Reaction: The patient reacted negatively, locally and generally, to all doses up to and including 7.5 mg. of old tuberculin.

Complement-Fixation Test for Tuberculosis: This was positive. (Done once only and by a commercial laboratory.)

Roentgenology: The entire body was radiographed and the following findings were obtained: The skeleton, aside from the bones of the hands and the feet,

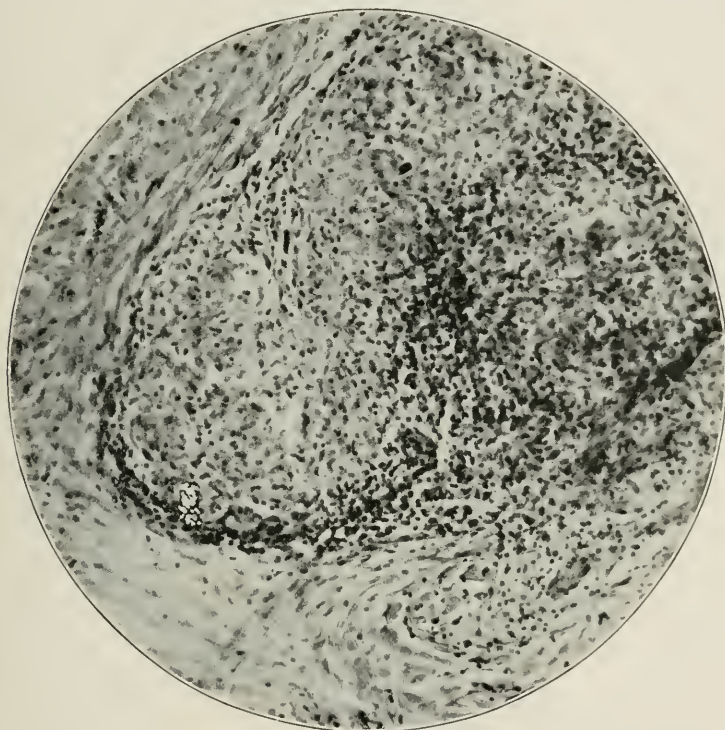


Fig. 4.—A lobule from the finger magnified 110 diameters, showing its epithelioid-cell composition and its dense plasma cell—round cell peripheral infiltrate.

was negative. Roentgen-ray examination of the feet showed circumscribed areas of central destruction in the distal ends of the fifth metatarsal and first phalanx of the first, second and fourth toes of the right foot and of the fifth metatarsal and first phalanx of the first and second toes of the left foot. There was no evidence of erosion from the outside in these bones. The bones of the hands showed areas of both central and cortical destruction. There was central destruction producing millet-seed to pea sized areas of reduced density in the distal ends of the first phalanges of the third, fourth, and fifth fingers and of all of the second row of phalanges, including a large pea-sized

area of reduced density in the shaft of the second phalanx of the index finger of the right hand. There was evidence of erosion of the cortex of the first and second phalanges of the middle finger. The left hand showed central destruction of the distal ends of the second, fourth and fifth metacarpals, of the first phalanx of the third and fourth fingers, of the second phalanges of the second and fifth fingers, and of the proximal end of the terminal phalanx of the fourth finger. There was marked cortical erosion of the shaft of the first phalanx of the fourth finger and of the second phalanx of the fifth finger.



Fig. 5.—Lesions on face.

Apparently the cortical erosion of these bones had resulted from the action of the tumors of the soft parts in contact with the bone. The central erosion was probably caused by tumors that had developed within the bone, as in many instances the cortex bordering on the areas of reduced density was nowhere perforated, as shown by anteroposterior and side views of the digits.

The heart and diaphragm shadows were normal, and there were no noteworthy shadows of the abdomen and pelvis. Moderately heavy hilum densities

were present with several (five in the left and about twelve in the right) small, dense nodules. There was moderately heavy, uniform, linear infiltration extending well toward the periphery throughout both lungs. This linear infiltration probably indicated an ancient chronic infiltrative process, as it was too uniform to denote a tuberculous involvement.

Bacteriology.—A piece of tissue was removed from each cheek, and the encapsulated nodule of the volar surface of the middle phalanx of the left little finger was excised in toto. Tissue was fixed in Zenker's solution and

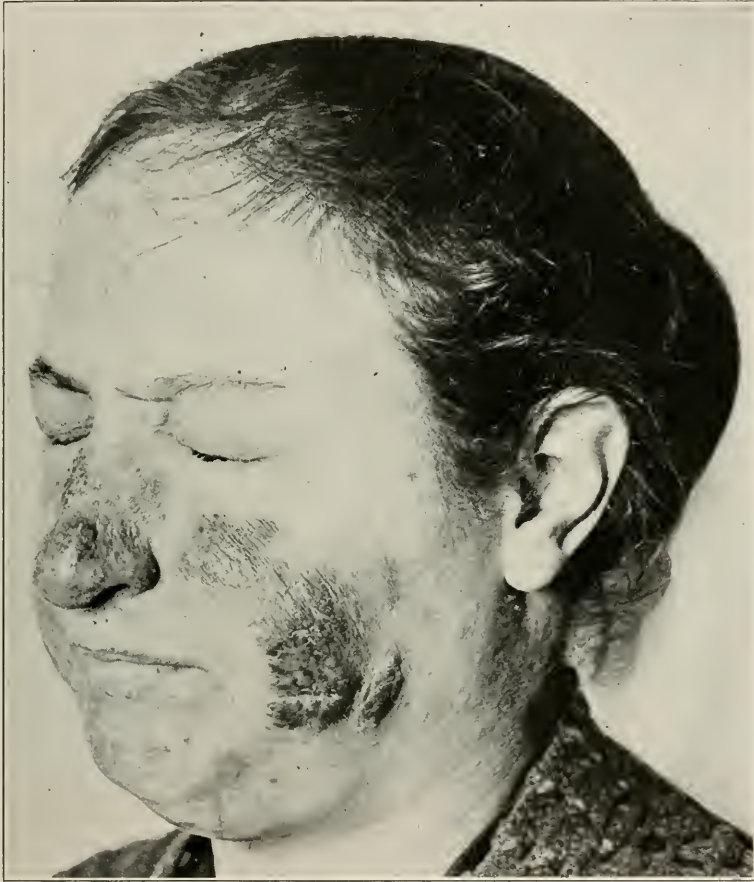


Fig. 6.—Lesions on face.

alcohol for microscopic study. The bulk of one of the cheek specimens and of the finger nodule was separately macerated in sterile salt solution in the grinder devised by Rosenow and injected into six guinea-pigs, three of each, intraperitoneally and subcutaneously. One pig died in thirty-seven days, after the gradual loss of considerable weight, of what appeared grossly and microscopically to be a nontuberculous bronchopneumonia, marked in both lungs. The other five pigs were killed sixty-two days after inoculation, four of them showing

definite pathologic changes but no evidence of tuberculosis, the fifth pig being perfectly healthy. Numerous tissue stains for tubercle bacilli and a search for the organism by the antiformin method were made of all tissues grossly altered, and in all instances with entirely negative findings.

Aerobic and anaerobic glycerine-agar and blood-agar cultures of tissues removed from the finger and face showed no bacterial growth in thirty-two days.

Histology.—The tissues removed from the face and the finger were blocked in paraffin and stained with hematoxylin eosin, Pappenheim's pyronin methyl green, Unna's polychrome methylene blue, Unna's orcein, Van Gieson's picric acid fuchsin alum hematoxylin, Weigert's resorcin fuchsin ferrisquichlorid, and Weigert's lithium carmin anilin methyl violet.

Over a hundred sections from the excised tissues were carefully examined for tubercle bacilli by the Ziehl-Neelson-Gabbet carbolfuchsin methylene blue



Fig. 7.—Lesions of the upper extremities and swelling and deformity of hands.

stain with disappointing results, although in several instances suspicion was aroused in the vicinity of giant cells, in each, undoubtedly, by artefacts. No granules were demonstrated with Much's modified Gram stain.

The finger nodule was densely encapsulated and relatively avascular. Coarse lobes of greatly varying sizes were formed by heavy connective tissue bands, and there were lobules within these formed by delicate collagenous bundles and a heavy round cell—plasma cell infiltrate. Within the lobes were chiefly large epithelioid cells and a few lymphocytes and ordinary connective tissue cells. There were no giant cells. The mast cells were occasional and limited to the periphery of the lobules, while the plasma cells were, as mentioned, not only abundant in this location, but also scantily interspersed among the epithelioid

cell proliferation. Elastic tissue was absent within the lobes, being clearly demonstrable only at the periphery and in the blood vessel walls. The overlying epidermis and upper corium of the nodule were not removed.

The sections prepared from the lesions of the face differed markedly from those described in that there was no dense connective tissue proliferation in the growth. The epidermis was apparently affected only secondarily, that is, by the pressure of the growth beneath it. It was decidedly thinned out and its rete pegs were practically obliterated, as were the adjacent papillae of the corium. The blood vessels of the corium were much dilated and increased in number, their walls evidently without noteworthy proliferation. There were grouped masses of fibroblasts in the upper portion of the corium and evidence of uniformly distributed older connective tissue also increased in this locality. The new growth was practically limited to the lower half of the *pars reticularis* and the hypoderm. It consisted of nests, rather confluent in places, of large



Fig. 8.—Deformity of hands and fingers.

epithelioid cells with pale-staining, large, vesicular nuclei. In the center of from one to three of these clusters of each section was what closely resembled a noncaseating miliary tubercle, the giant cells being chiefly of the Langhans type. Interspersed in these nests were a few plasma and ordinary connective cells, as well as a few small mononuclear leukocytes. These epithelioid clusters were separated from those adjacent by delicate collagenous strands and a heavy plasma cell—round cell infiltrate containing an occasional mast cell. The granuloma itself was relatively avascular, the only vessels present being at the periphery of the lobules where the infiltrate was most marked. Elastic tissue was demonstrable only at the periphery of the lobules and in the blood vessel walls. Clumps of interwoven strands of fibrin were demonstrable here

and there in fair abundance. There was no evidence of necrosis in any part of the sections or of invasion or pressure atrophy of gland, nerve, or blood vessel structures. The lymph spaces were apparently dilated in most parts of all of the sections, but were without proliferation and without recognized relation to the cell infiltrate.

Treatment.—There has been no response to prolonged arsenical medication per os, the patient having taken large doses constantly for a period of two years. Roentgen-rays have been extensively used on the hands and face without permanent improvement. Recurrence has taken place in all of the lesions excised, even the scar being almost completely replaced by the growth. Arsphenamin and tuberculin injections are yet to be employed. The lesion of the manubrium has recently been destroyed, apparently entirely, with radium, only atrophy and pigmentation remaining.

DISCUSSION

The case under consideration is of special interest because: 1. It is associated with bone involvement. 2. It is of mixed type (Boeck and Darier-Roussy). 3. There are no definite concomitant tuberculous findings. 4. There is no response to prolonged therapy of the varieties generally employed in these cases with some or much success.

There can be no doubt that the diagnosis is correct, not only because of its classical histopathology, gross appearance and history, but also because it has been undisputed after observation by numerous well-known dermatologists from all parts of the country, the case having been repeatedly shown before the Chicago Dermatological Society at regular and annual meetings.

The patient has been under the observation of Dr. Oliver S. Ormsby and Dr. James Herbert Mitchell for over two years, and it is to them that the author is indebted for the privilege of studying the case. For the skiagraphy, the author is indebted to the kindness of the Presbyterian Hospital of the City of Chicago and for the interpretation of the plates to Dr. D. B. Phenister of this city.

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FOUR CASES OF LICHENOID TRICHOPHYTIDE *

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The occurrence of a systemic reaction accompanied by a more or less generalized eruption in severe cases of tinea, especially kerion of the scalp, has been noted with increasing frequency in European literature, but as yet has received only scant attention in this country. Bloch¹ has published several articles on the subject, the last one giving a number of illustrative cases and containing a very illuminating discussion of the phenomena so far observed in this connection and of the theories adduced to account for them. Appended to this article is an extensive bibliography. Rasch² also has recently published an analysis of cases of the same kind observed at Copenhagen. These workers, and others also, have noticed that in some cases of severe kerion, either of the scalp or the bearded face, there is a systemic reaction, with fever and more or less prostration, and accompanied by a more or less generalized eruption, occurring usually after the kerion has been in existence for a considerable time.

Cultures have shown that the fungus causing the kerion may be any one of several species, and there seems to be no relationship between the variety of fungus and the character of the secondary eruption. All that is required is that there should be a deep and extensive mycotic inflammation. The commonest form of exanthem is an eruption of small, lichenoid papules, sometimes occurring singly, but usually grouped in patches of varying size. Other types have been noted, however, vesicles, pustules, a scarlatina-form rash, erythema multiforme, and nodes like those of erythema nodosum. It has been noted that in patients suffering from kerion, the injection of trichophytin may produce an eruption exactly like that occurring in the course of the disease. These eruptions all fade as the kerion heals, and if there be any areas of tinea on the skin these also heal without treatment. The entire skin, in severe cases of kerion, seems to have become hypersensitive to the poisons produced by the disease, and as these increase in quantity the organism acquires an immunity by virtue of which it throws off the infection from its original site and also from any secondary foci that may have developed.

* From the New York Skin and Cancer Hospital.

1. Bloch, Bruno: *Ann. de dermat. syph.* **2**: (Jan and Feb.) 1921.

2. Rasch, C.: *Brit. J. Dermat.* **32**: 317 (Nov.) 1920.

REPORT OF CASES

CASE 1.—*Examination.*—L. C., a girl, aged 6 years, came to the New York Skin and Cancer Hospital, March 18, 1921, suffering from a severe infection with pediculosis capitis. Closer examination revealed a severe and extensive kerion. On March 21, she had a profuse eruption involving the trunk and upper extremities, the primary lesion of which appeared to be a tiny red papule. The brightness of the color suggested scarlatina, but the papules were too large and the distribution too uneven. These papules occurred in part singly, but mostly in groups varying in size from half an inch to several inches in diameter. The groups were very irregular in outline and showed no tendency to form distinct marginate patches or to clear in the center. The conjunctivae were congested, the tongue distinctly reddened and the temperature was 103.2 F.

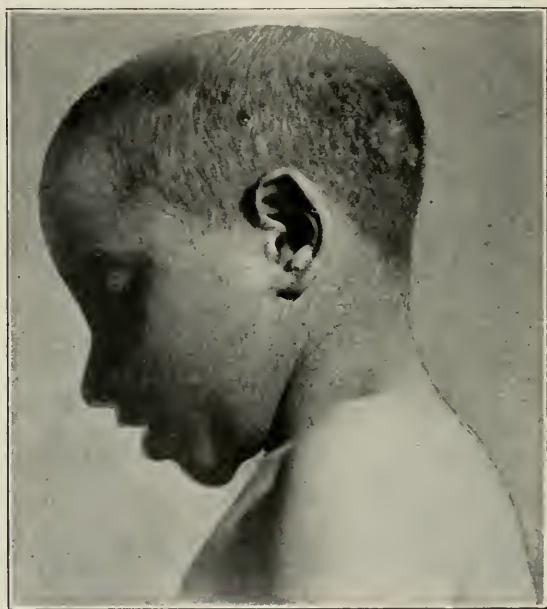


Fig. 1.—Patient in Case 2, showing kerion of occiput and follicular trichophyite of the side of the neck.

Subsequent Course.—She was treated at home by the visiting nurse of the hospital, and on April 4 the pediculosis was cured, and the kerion was subsiding, but the eruption persisted. At that time the scalp had been cleared of vermin, but showed many scattered irregular bald areas, somewhat boggy in the center. The exudation of pus had ceased. Spores and fragments of mycelia were not found in the hairs and scales. On April 11, the eruption on the body had faded somewhat, having changed its color from a bright red to a reddish brown, so that in many places it bore a close resemblance to a grouped follicular syphilid. The temperature had fallen, and the patient was evidently convalescent. Many hairs were examined the same day, but, although they were loose and easily extracted, only one showed any sign of ringworm infection. Some of the scales from the scalp showed spores.

Summary.—To summarize, we have here a case of severe kerion accompanied by fever, prostration, and a diffuse exanthem, going on to spontaneous healing, all symptoms subsiding together.

CASE 2.—History.—H. W., a boy, aged 9, born in New Jersey, came under treatment May 17, 1921, for a ringworm which had developed about a month previously on the occiput, 2 inches behind the left ear, and which soon involved the rest of the scalp. Within the last week an erythematous-papulo-squamous eruption had spread over the right side of the face, neck and chest. A week before the whole scalp was badly swollen. The patient had been feverish for from eight to ten days, and very restless, especially on May 9.

Examination.—The original spot on the occiput, about an inch in diameter, was bald and crusted, showing some broken hairs, and a moderate degree of



Fig. 2.—Sister of patient in Case 2, showing typical tinea circinata of shoulders.

exudation. There were other lesions on the scalp about a quarter of an inch in diameter, with crusts from one sixth to one eighth inch in thickness. The "trichophytide" involved the entire face and neck, being most marked just behind and below the left ear, where the skin was red, tumefied, rough, dry, and covered with fine scales. The eruption faded toward the periphery, where there were small follicular papules, often capped with fine scales. In front, the eruption extended down as far as the level of the left nipple. In the midst of this papular rash in the neck were two oval spots about half an inch long, resembling tinea circinata; but no organism was found in the scrapings.

The sister of this patient had a typical tinea circinata on each shoulder. Spores were demonstrated in hairs from the boy, and mycelia in scales from the girl's shoulder.

CASE 3.—History.—H. B., a boy, aged 9 years, came under treatment May 18, with a history of tinea of about eight weeks' standing, and kerion of from three to four weeks' standing, but most acute during the early part of May. There had been much swelling of the scalp, especially of the right side, accompanied with exudation of sero pus. For the past three weeks, the child had been restless and feverish at night, and he had a poor appetite.

Examination.—The kerion was about 2 inches in diameter, with a few outlying spots. Spores were demonstrated in the hair. There was no eruption on the body.

Subsequent Course.—On May 18, the kerion was subsiding. Surrounding the neck, most marked on the sides, was an eruption of small soft follicular papules. Those at the border of the area were flesh colored, the others becoming a deeper red and more elevated toward the center of the area involved. There were some urticarial lesions on the forearm. On May 20, urticarial lesions were still visible on the forearm, but the papules on the neck were fading.

CASE 4.—History.—R. L., a white boy, aged 10, American born, was first seen March 26, 1921. The duration of the condition was about six weeks, a cat being the source of infection.

Examination.—On the left parietal region was a large kerion, the size of a silver dollar, which was tumefied. The surface showed alopecia and broken hairs. On the back of the neck and occiput were many vesico-pustules about one-eighth inch in diameter. A few of these lesions were also seen on the vertex. The occipital lymph nodes were considerably enlarged and tender. On the external surface of the right thigh, about 3 inches above the knee, was a round crusted lesion the size of a five-cent piece. The skin of the trunk and limbs was otherwise negative. There was no suggestion of keratosis pilaris, of lichenoid lesions, or of seborrheic dermatitis.

Subsequent Course.—On April 5, the condition of the kerion was better. The occipital glands were more swollen and tender; the follicular condition of the scalp was worse, there being now many more vesico-pustules, involving the whole scalp, with a few below the hair line of the forehead and temporal regions, and many on the back of the neck. There were no lichenoid lesions on the face or limbs. The mother stated that the child had been feverish at times. The temperature at 7:30 p. m. was 98.3 F.

On May 2, 1921, the mother stated that the child was quite sick after the last visit. He complained of being chilly, and the skin felt hot and dry. His appearance showed this.

The kerion was very much improved; the nodes not quite so swollen or tender. The whole scalp was covered with vesico-pustules. At the base of the neck, and on the axillary folds, the back and the legs, were a few irregular groups of lichenoid lesions, suggestive of lichen scrofulosus, which the mother claimed had been present a week or ten days. She stated that they were less marked and seemed to be resolving. On May 18, the kerion was much better and the lesions on the body were practically gone.

Comment.—The case shows, in addition to the lesions caused by the direct action of the fungus, two types of eruption—the vesico-pustules on the scalp, forehead and neck, and the lichenoid papules on the rest of the body.

My thanks are due to Dr. Whitehouse and Dr. Throne for the privilege of reporting Cases 2 and 4. This series of cases is presented as a preliminary report in the hope of calling attention to a type of

eruption which is probably more common than we have believed and which has not been recognized because it has not been looked for. Cultures have been made from all the cases, but up to the present time a growth has been obtained only from Case 4. This shows an organism resembling the *Trichophyton faviforme*, but differing from any recognized variety.

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OPTIMUM CONDITIONS OF FIXATION OF COMPLEMENT IN THE WASSERMANN TEST *

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An investigation of the rate of fixation of complement at different temperatures carried out with protein antigens and specific immune rabbit serums, reported elsewhere,¹ led to the following conclusions:

1. The rate of fixation of complement is approximately the same at icebox (6 to 12 C.), room (18 to 25 C.), and water-bath (37.5 C.) temperatures, the tendency being for somewhat greater fixation at icebox temperature.

2. From 60 to 80 per cent. of complement is "fixed" during the first hour of fixation at either icebox, room, or water-bath temperature, the amount being directly proportional to the number of antibodies in the immune serum, fixation being completed in about four hours at icebox temperature.

The fixation periods at water-bath and room temperatures were not extended in these experiments beyond two hours, in view of the deterioration of complement after prolonged exposure at these temperatures.

The proteins used in these studies were edestin from hempseed and phaseolin from the kidney bean, kindly furnished by Dr. Thomas B. Osborne of the Connecticut Agricultural Experiment Station.

A study of the velocity of fixation of complement at different temperatures in the Wassermann test was next undertaken. A detailed presentation of this work will be given elsewhere. Briefly, this investigation was carried out with six different antigens: (1) a crude alcoholic extract of guinea-pig hearts; (2) a crude alcoholic extract of beef hearts; (3) an alcoholic extract of beef hearts previously freed from ether-soluble lipoids; (4) the same antigen cholesterinized with 0.4 per cent. cholesterol; (5) a Noguchi antigen; and (6) a human heart antigen cholesterinized with 0.4 per cent. cholesterol. The periods of fixation were 0, 5, 15, 30 and 60 minutes, and 2, 3, 4, 5 and 6 hours. The fixation temperatures were, as in the case of the protein antigens, icebox, room and water-bath.

* From the Bureau of Laboratories, Michigan Department of Health, Lansing, Mich. Presented before the Eighth Annual Meeting of the American Association of Immunologists at Cleveland, Ohio, March 24, 1921.

1. Kahn, R. L.: *Proc. Soc. Exper. Biol. & Med.* **18**:168, 1921. Complete report to appear shortly in *J. Exper. M.*

It was found with these antigens, with the exception of the Noguchi antigen, that the velocity of fixation of complement at these temperatures was approximately the same, the tendency being for somewhat greater fixation at icebox temperature. The velocity of fixation with the Noguchi antigen was somewhat greater at water-bath than at icebox temperature. The fixation periods at water-bath and room temperatures were in these experiments, also, not extended beyond two hours.

It was further found that the velocity of fixation of complement was directly proportional to the concentration of the so-called syphilitic antibodies in the syphilitic serums, and that maximum fixation was attained in about four hours at icebox temperature.

The problem that presented itself as a result of the foregoing studies—and which I shall discuss—was to establish whether these experimental findings would be applicable to the routine Wassermann tests carried out in this laboratory, particularly whether icebox fixation could safely be substituted for water-bath fixation in the case of the cholesterinized antigen tests and whether there would be any advantage in it.

EXPERIMENTAL

Until Feb. 9, 1921, we made duplicate Wassermann tests with two antigens and two modes of fixation on all specimens received for examination, employing a period of four hours' fixation in the icebox in the case of the alcoholic antigen tests, and a fixation period of forty-five minutes in the water-bath in the case of the cholesterinized antigen tests. Of about 20,000 Wassermann tests carried out with these two modes of fixation, the tendency has been for weaker reactions with the cholesterinized antigen and water-bath fixation, as compared with the alcoholic-antigen tests. The same specimens which gave a + + + + reaction with the alcoholic antigen after four hours' fixation in the icebox, frequently gave a + + + reaction with the cholesterinized antigen and forty-five minutes' fixation in the water-bath. One which gave a + + + reaction with the alcoholic antigen occasionally gave a + + or even + reaction with the cholesterinized antigen.

Early in February, a series of duplicate Wassermann tests were carried out with the cholesterinized antigens, employing forty-five minutes' fixation in the water-bath in one case and the same fixation period in the icebox in the other. The results of 100 such tests are recorded in the table. The tendency for slightly stronger fixation at icebox temperature is clearly shown.

Accordingly, on Feb. 9, 1921, we eliminated water-bath fixation with the cholesterinized antigens and substituted a fixation period of one hour in the icebox instead. This period was chosen instead of

forty-five minutes because the anticomplementary tendency of cholesterinized antigen observed with water-bath fixation is reduced to a minimum when icebox fixation is resorted to. It was further felt that one hour's fixation would not be likely to give false positive results with this antigen.

COMPARATIVE STUDY OF SYPHILITIC SERUMS TESTED WITH CHOLESTERINIZED ANTIGEN AT WATER-BATH AND ICEBOX TEMPERATURES

Serum Number	Fixation for 45 Minutes in the		Serum Number	Fixation for 45 Minutes in the	
	Water-bath	Icebox		Water-bath	Icebox
1	±	±	51	—	—
2	—	—	52	—	—
3	—	—	53	—	—
4	—	—	54	—	—
5	—	—	55	±	+
6	±	±	56	—	—
7	—	—	57	—	—
8	—	—	58	—	—
9	—	—	59	—	—
10	—	—	60	±	+
11	—	—	61	—	—
12	++++	++++	62	—	—
13	—	—	63	—	—
14	—	—	64	±	±
15	+++	++++	65	—	—
16	—	—	66	—	—
17	—	—	67	—	—
18	+	—	68	++++	++++
19	—	—	69	—	—
20	—	—	70	—	—
21	—	—	71	—	—
22	—	—	72	—	—
23	—	±	73	—	—
24	—	—	74	—	—
25	÷	+	75	+	+
26	—	—	76	—	—
27	±	±	77	—	—
28	—	—	78	—	—
29	—	—	79	—	—
30	—	—	80	—	—
31	+	++	81	—	—
32	—	—	82	—	—
33	++	++	83	—	—
34	±	±	84	++++	++++
35	+++	+++	85	++++	++++
36	—	—	86	—	—
37	—	—	87	—	—
38	±	±	88	—	—
39	—	—	89	—	—
40	—	—	90	—	—
41	+	÷	91	—	—
42	—	—	92	—	—
43	++++	++++	93	—	—
44	—	—	94	±	±
45	—	—	95	—	—
46	—	—	96	—	—
47	+++	++++	97	++++	+++
48	—	—	98	—	—
49	—	—	99	—	—
50	—	—	100	—	—

Of 6,000 Wassermann tests performed with the cholesterinized antigen and one hour's fixation in the icebox, the results approximate the alcoholic antigen tests with four hours' fixation more closely than when the cholesterinized tests were carried out with water-bath fixation. A small percentage of specimens show a tendency for slightly stronger fixation with the cholesterinized antigen; then again, an equally small number show a tendency to slightly stronger fixation with the alcoholic antigen.

Regarding our Wassermann procedure, it might be stated that a sheep cell system is employed. The quantities are one tenth of the original Wassermann technic. All reagents entering into the test are measured in 0.1 c.c. quantities, except the patient's serum, which is employed in quantities of 0.01 c.c. and 0.02 c.c. Two units of complement and 2 units of amboceptor are employed and from 8 to 10 antigenic units in the case of the alcoholic extract antigen and from 3 to 4 antigenic units in the case of the cholesterinized antigen. For further details the reader is referred to other papers from this laboratory.²

DISCUSSION

The fact that the velocity of fixation of complement in the Wassermann test is about the same at icebox or water-bath temperature, and that fixation of complement is completed in about four hours suggests the possibility that those who employ a one-half or one hour period of fixation in the water-bath do not obtain the maximum amount of fixation. It is true that strongly positive syphilitic serums show marked fixation of complement after from five to fifteen minutes. In the case of weaker positives, however, no more than 50 per cent. of fixation is frequently obtained after one hour as compared with four hours' fixation.

The question of the period of fixation necessary to obtain the maximum sensitiveness of the cholesterinized antigen, without picking up false positives, is a problem in itself. We are inclined to agree with Smith and MacNeal,³ Ottenberg⁴ and others⁵ that prolonged periods of fixation with cholesterinized antigen will occasionally pick up a false positive result and, therefore, limit the fixation period with this antigen to one hour. We are not, however, in agreement with those workers as to the temperature of fixation, preferring the icebox to the water-bath.

The main advantage of icebox over water-bath fixation in the case of the cholesterinized antigen lies in the fact that the former procedure renders the antigen less anticomplementary as compared with the latter. The tendency for anticomplementary properties, which is inherent with the cholesterinized antigen, is reduced to a minimum when a one hour icebox fixation period is employed. A probable explanation for this is that a small amount of complement deteriorates during water-bath fixation, while the complement is practically preserved in the icebox.

2. Kahn, R. L.: *J. Lab. & Clin. M.* **6**:153 and 218, 1920 and 1921, and forthcoming issue. *Am. J. Pub. Health* **11**:410, 1921.

3. Smith, J. W., and MacNeal, W. J.: *J. Infect. Dis.* **21**:232, 1917.

4. Ottenberg, R.: *Arch. Int. Med.* **19**:457, 1917.

5. Owen, R. G., and Martin, F. A.: *J. Lab. & Clin. M.* **5**:232, 1920.

Our studies indicate further that the velocity of fixation with cholesterinized antigens is somewhat greater than with alcoholic antigens. This undoubtedly explains why our results with the cholesterinized antigens and one hour fixation approximate the results of the alcoholic antigen tests after four hours' fixation.

Kolmer and co-workers,⁶ who have made a careful study of the effects of temperature and time on fixation of complement, conclude that "The (fixation) method of choice narrows down to a selection of three or four hours at 8 to 10 degrees C. plus one hour in the water-bath at 38 degrees C. or eighteen hours at 8 to 10 degrees C. The latter is preferred on the basis of somewhat more sensitive reactions, but the differences are not marked."

Judging from our experience with the technic employed in this laboratory, the slight increase in the amount of complement "fixed" after 5, 7 and 9 hours' fixation, as compared with four hours, is largely nonspecific, due, most likely, to the deterioration of complement. We do not doubt that eighteen hours' fixation will result in a more sensitive reaction than four hours. But this increase in sensitiveness, judged from our studies is largely nonspecific, and a fixation period of twenty-four hours would, in our opinion, for the same reason result in a more sensitive reaction than eighteen hours.

CONCLUSIONS

1. The optimum conditions of fixation of complement in the Wassermann test with alcoholic-extract and Noguchi antigens appear to be four hours at ordinary icebox temperature (from 6 to 12 C.).

2. With cholesterinized antigens, a one-hour fixation period at icebox temperature is recommended. Icebox temperature renders the reactions somewhat sharper than water-bath temperature, and a one hour period precludes the possibility of picking up false positive reactions with these antigens.

6. Kolmer, J. A.: Matsunami, T., and Trist, M. E : *J. Syph.* **5**:63, 1921.

AN EXPERIMENTAL VERIFICATION OF THE SIGNIFICANCE OF THE DELAYED NEGA- TIVE WASSERMANN REACTION

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AND

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Several years ago, Olson¹ and more recently, McConnell² have called attention to a phenomenon known as the "delayed negative" Wassermann reaction. In essence, it has to do with the time at which the reaction is read. If read in about thirty minutes, it is positive; but at the end of an hour or two hours, as the case may be, it is negative. They are inclined to the opinion that such a reaction should be regarded as at least a partial one. McConnell has shown that it occurs in about 1 per cent. of his cases, which he has divided into three groups: the first group comprises known syphilitic patients, most of whom had received treatment; the second, those who probably had syphilis, and the third, those presenting no evidence of syphilis. As is to be expected, the greatest percentage of these reactions is to be found in the first group.

In this connection, however, it is worthy of note that Strickler,³ Munson and Sidlick have observed that arsenic itself may produce a positive Wassermann reaction when administered to patients suffering from diseases other than syphilis. The significance of this fact is of course obvious, as it has been common practice to use the Wassermann reaction itself as a control to treatment, and to regard the partial reactions obtained after treatment as an indication of decreased activity on the part of the disease. Personally, I have never been able to believe that this apparent correlation was very well founded, knowing as little as we do about the actual mechanism of complement fixation. The fact that arsenic administration is often followed by a disappearance of the earlier lesions of syphilis is not sufficient ground for drawing conclusions regarding a connection between the absence of a Wassermann reaction and the latency or disappearance of the disease itself.

1. Olson, G. M.: The "Delayed Negative" Wassermann Reaction, *J. Lab. & Clin. Med.* **1**:704, 1916.

2. McConnell, G.: The "Delayed Negative" Wassermann Reaction, *ibid* **5**:43, 1919.

3. Strickler, A.: A Positive Wassermann Test in Nonsyphilitic Patients After Intravenous Therapy, *J. A. M. A.* **75**:1488 (Nov. 27) 1920.

Attempts to increase the delicacy of the Wassermann reaction for diagnostic purposes are worth while, although such attempts have usually introduced the nonspecific factor. The probable freedom of the "delayed negative" phenomenon from that implication would add greatly to its value from the standpoint of increased delicacy. To my knowledge, no observations have been recorded in which the connection is particularly direct. For this reason I desire to record the following observation, which concerns complement fixation as it occurred in a patient suffering from blastomycosis and in animals experimentally infected.

In this case we were able to isolate three distinct varieties of *Oidium* from the various lesions, and we were interested to know whether the patient's serum contained bodies immune to more than one of them. The whole study will be made the subject of a special communication in the future. The antigens were prepared from thoroughly washed suspensions of the organism, which had been grown from 48 to 72 hours on agar slants. After the washing, they were killed with 0.25 per cent. formol. They were not anticomplementary or hemolytic, and their fixing power was fair. A suspension was prepared, of such turbidity as to give a quantity of 0.1 c.c. for the antigenic unit, which was one fourth of the anticomplementary dose. The patient's serum was used in 0.15 and 0.3 c.c. quantities, and was run side by side with the serum of rabbits which had received three injections of the live organisms.

The control rabbit serum and normal human serum came down promptly at the end of fifteen minutes; but at the end of thirty minutes, the reaction of both the immunized rabbit and the patient was ++++. At the end of forty-five minutes, a marked hemolysis developed, which at the end of the hour left the reaction approximately + or doubtful. At the end of twenty-four hours the reaction was unchanged, and it was perfectly obvious that there was indeed a slight inhibition. More precisely, the reaction in this case should be styled a delayed doubtful, but probably the phenomenon is essentially the same.

We wish to call attention to the fact that the rabbits used were inoculated with pure living cultures of one type of the organism, freshly isolated from the patient's lesions. Some of them succumbed to the infection, as was definitely proved at necropsy and by culture, while others, which had received smaller doses, were made very sick. This was shown by a pronounced drop in weight which they failed to regain after a period of two months. Moreover, they were scrawny and gave the impression that they might die at any time. The blood used in the test was drawn after a period of two months from animals that were definitely proved to have blastomycosis. Their serum was

inactivated at 62 C., as Kolmer⁴ has shown some time since that this temperature destroys the tendency for nonspecific reaction which occurs at times with these animals.

The fact that in the serum both of the patient and of the immune rabbits we obtained this delayed doubtful or practically negative reaction, when it was definitely known that both were suffering from the blastomycotic infection, seems significant in the interpretation of this type of reaction. It is always a step toward understanding an obscure process to put it alongside of another which is similar to it and which may be more amenable to experiment. It is obvious that, short of a spirochete demonstration, it is not possible to make a positive diagnosis of syphilis with finality in the individual case.

It is of interest also that the patient's serum showed definite agglutination to two of the three types of yeasts with which it was tried, although this occurred in a dilution of 1:1. It was completely negative in dilutions of 1:25. However, the control with normal serums was entirely negative, and the results are in accord with those originally reported by Ricketts⁵ in his study of blastomycosis.

It is likewise of importance that control titrations of the positive serums with an antigen prepared from *Endomyces albicans* were negative within the quantitative limitations of the test as employed. The latter yeast strain was isolated by Tanner⁶ from an ordinary pyogenic infection of the finger.

The tendency, then, to regard the delayed negative Wassermann reaction as essentially positive is strengthened by the appearance of the same phenomenon in a patient and in animals definitely proved to have been suffering from blastomycosis.

4. Kolmer, J. A., et al: Studies in Nonspecific Complement Fixation, J. Infect. Dis. **18**:20, 1916.

5. Ricketts, H. T.: Oidiomycosis (Blastomycosis) of the Skin and Its Fungi, J. Med. Res. **6**:377, 1901.

6. Tanner, F. W., and Feuer, B.: Cultural Studies on an Infection of the Skin by *Endomyces Albicans*, Arch. Dermat. & Syph. **1**:365, 1920.

ONYCHIA DUE TO BACILLUS COLI COMMUNIS

LESTER HOLLANDER, M.D.

PITTSBURGH

Two cases of onychia have come under my observation within the last twelve months in which cultures from the purulent material obtained from the nail bed yielded practically a pure strain of *Bacillus coli communis*.

REPORT OF CASES

CASE 1.—*History*.—Mrs. A. J. H., aged 52, was referred to me on account of a chronic onychitis affecting three nails on the right hand and one nail on the left, of about five months' standing. The patient did not remember definitely any injury to the nails or to the nail fold. The first symptom which attracted her attention was a severe burning sensation in two of the fingers at the nail bed. She did not notice any change in color, nor was there any visible swelling at this time. The burning sensation had increased from time to time until about three weeks after the onset, when the nail fold over the nail bed became red and considerably swollen. On the advice of a physician, the patient applied hot fomentations of boric acid solution, but did not experience any relief. The burning sensation was supplemented by considerable pain and throbbing, especially at night. In the morning she could press out a little pus from the nail fold and obtain some relief. Within another month, another nail bed on the right and one on the left hand became involved.

Examination.—The distal phalanges of all the involved fingers were swollen and red. On pressure over the nail bed a purulent material was obtained. The nail wall was inflamed and the involved nails were thickened, uneven, and considerably loosened from the nail wall.

Culture from the expressed pus yielded *B. coli communis*.

Treatment.—The nail bed was incised along the margin of the nail wall, and compresses of the following solution were applied continuously for one week, and only at night for another week, with complete recovery.

	Gm. or c.c.
R Hydrargyri Oxidi Flavi.....	0.065
Potassii Iodidi	0.260
Aquae purae	q. s. ad. 100.000

CASE 2.—*History*.—Mrs. I. S., aged 40, was referred to me on account of a similar complaint. Both thumbs and all the fingers were involved in a chronic onychitis. The distal phalanges were markedly swollen, and the nails were rough, uneven, very brittle, and of a dark brownish, dirty color. The trouble was of a year's standing and very annoying, not only from a cosmetic standpoint, but also because it interfered with the patient's housework, because of the extreme sensitiveness experienced, following the use of her hands. She could not remember any injury from manicuring, or other type of trauma to her fingers. The patient was very emphatic in the statement that she began

to experience a burning sensation in all her finger tips at about the same time and that the visible changes in the nail folds appeared almost simultaneously within a few days after the annoying sensation developed.

Examination.—After incising the nail beds, the pus was separately cultivated and the offending organism in all the cultures proved to be *B. coli communis*.

Treatment.—This patient complained of frequent headaches, marked constipation, and of a constant languid feeling.

The treatment used in Case 1 failed to effect a permanent cure. So, after several surgical drainings, an autogenous vaccine was made and administered.

This produced a marked change not only in the onychitis, but also in the general condition, including the constipation.

COMMENT

These two cases permit the assumption of two different routes of conveyance of the infecting organism. The first case, presenting no general symptomatology and a rapid relief after surgical interference, may have been a contact infection, while the second case, an autogenous one, through the hemotogenous route.

7133 Jenkins Arcade Building.

A NOTE ON THE TREATMENT OF LARVA MIGRANS

LLOYD W. KETRON, M.D.

BALTIMORE

Since the parasite causing creeping eruption lies in the skin some distance from the end of the visible burrow, its demonstration is difficult, either for the study of the insect itself or for its destruction. The usual methods that have been resorted to in destroying the larva have been the injection of various cauterizing agents, or excision, both of which have frequently been unsuccessful.

Crocker failed to cure his patient after injection of iodine and phenol and had to resort to excision.

Hutchins was able to destroy the larva by cocainizing the region about the end of the burrow and injecting chloroform.

Hartzell succeeded by applying chloroform over the end of the advancing burrow ten minutes at a time, several times daily.

Stelwagon treated four patients and cured them all by applying cataphoretically a solution of mercuric chloride (2 grains to an ounce) around the edge of the burrow and touching the suspected site of the insect with nitric acid.

The method which I shall describe, however, seems to offer decided advantages over the usual ones both in effectiveness and simplicity. Although I have not made an extensive survey of the literature, I have found no mention of it in a number of modern textbooks on dermatology. If it should have been published before, the fact that it is not generally known will justify the repetition.

REPORT OF A CASE

History.—The patient was a young man, 28 years of age, who spent two weeks in August of 1920 at Stone Harbour, N. J. During this time, while fishing, he waded around in the sand and mud, often in his bare feet. He soon felt some soreness of the bottom of the foot which was later affected, and he thought that he had a stone bruise. He returned to Tolchester, Md., and while bathing there was bothered with considerable itching of this foot; he noticed that it was very red.

Treatment and Course.—I first saw him about one week after this, made the diagnosis of larva migrans, and advised his physician to use some of the usual methods of treatment. These, however, were unsuccessful, and the patient came to me a few weeks later and was under my care for about two months. During this time it was definitely established that there were two larvae. One was operating in the instep region of the sole of the foot and the other further forward near the base of the toes. Attempts were made to

destroy the insect by application of pure phenol, but this was unsuccessful. Later alcohol was injected, but this procedure also did not meet with success. I was also unable to find the parasite by opening the active end of the burrow with a fine scalpel.

Finally, an area the size of a twenty-five cent piece around the end of the burrow was frozen solid with ethyl chlorid. The patient returned in about two weeks and reported that the treatment apparently had been successful. The other larva was handled in the same manner also with apparent cure. A late communication from the patient about three months after the treatment, stated that he had had no further trouble with the condition. The freezing of the tissues caused practically no local reaction or discomfort.

SUMMARY AND COMMENT

A case of larva migrans is reported in which two insects were present in the sole of one foot. Both insects were destroyed by once freezing a 25-cent-sized area around the advancing end of the burrow.

If this treatment should prove a success in other cases, it offers advantages of simplicity and rapid effectiveness over the usual methods.

Obituary

SARAH ELIZABETH FINCH, 1881-1921

Dr. Sarah Elizabeth Finch, of Sound Beach, Connecticut, died in the Lenox Hill Hospital, New York City, on June 21, 1921, in her fortieth year. She graduated from Syracuse University in 1900, and from Cornell University Medical College four years later.

At the time of her death, and for many years previously, she was connected with the New York Skin and Cancer Hospital. She was greatly interested in skin diseases in young children, and she had charge of the outpatient work for babies at the hospital. She was making genuine progress in distinguishing between fact and fancy in the problem of feeding cases of infantile eczema. She was assistant pathologist to the hospital. She was particularly interested in bacteriology and mycology of the skin, and in her work she had struck leads which gave great promise of ending in the solution of some of the problems of the etiology of certain obscure dermatoses. There were few workers in America so familiar with the trichophytons and allied organisms. She has done much careful work on mycosis fungoides and on Hodgkin's disease. It is to be hoped that some of her researches have been left in such shape that they will not be lost.

She was conscientious, careful and essentially scientific, and was unwilling to express opinions until she felt sure of her ground. She was one of those faithful workers who do so much and get so little credit. Dermatology has lost in Dr. Finch's death a thorough and useful disciple, and her co-workers an associate who will be greatly missed.

X.

Correspondence

"OBSERVATIONS ON MEDICAL PHOTOGRAPHY"

To the Editor:—After having read with great interest the "Observations on Medical Photography" by Dr. Fox in the July issue of the ARCHIVES, I am sure that he will pardon me if I offer a suggestion to the "youngsters" of the profession who are unable to buy and to operate an expensive camera.

I have found that excellent photographs, giving good detail even in such small lesions as verruca of the face, can be made by the use of the ordinary 3A Eastman folding kodak with a rapid rectilinear lens, using in addition a suitable portrait attachment.

With correct distance, according to the chart enclosed with the portrait attachment and the proper exposure, photographs can be made which add greatly to the value of the case record, giving in addition a guide to the progress of the disease.

The picture made by the kodak is of a convenient size, $3\frac{1}{4}$ by $5\frac{1}{2}$ inches, from which enlargements to any ordinary size can be made. In addition to the low cost (about seventeen cents per picture including cost of film, developing and printing) the developed film can be filed for reference in a much smaller place than a plate and of course is not liable to be broken.

Although all photographs that I have taken have been made by short time exposure in a well lighted office, I see no reason why with a little care equally good results could not be obtained by flashlight.

JAMES W. ANDERSON, M.D., Norfolk, Va.

Abstracts from Current Literature

MULTIPLE MALIGNANT NEOPLASMS. L. J. OWEN, J. A. M. A. **76:**
1329 (May 14) 1921.

Owen considers only multiple malignant growths arising from primary foci, carefully excluding all cases in which the possibility of metastatic lesions or recurrences was present. In all cases possible a study of the pathology of the tissues was made, and of the cases in which this was not possible only those in which a definite clinical diagnosis could be made were included. The literature of multiple malignant neoplasms is small, if cancer of coal tar workers and xeroderma pigmentosa are excluded. These two diseases were not considered in this study.

Three thousand cases of malignancy were reviewed, and 143 cases, or 4.7 per cent., of multiple growths were collected.

Multiple basal cell cancers were observed in eighty-six cases. The lesions were found nearly always on exposed surfaces, and in every instance there was at least one carcinoma on the upper part of the face or scalp. Twenty-five per cent. of the patients in this group were farmers. Exposure is apparently a potent factor in the development of this disease.

The coincidence of basal cell and prickle cell cancers was observed twenty times. The distribution of the basal cell tumors in this group was comparable to that of the preceding group, while the more malignant tumors arose from the mucous membrane of the mouth in seven instances, six times from the face other than the lip, three times from the mucocutaneous border of the lower lip and in four cases from the hands.

Multiple malignant squamous cell carcinomas were observed seven times. There were five cancers of the mucous membrane seen in three patients in this group, the remaining growths being prickle cell in type.

Fourteen patients presented bilateral cancers of the breasts. Simultaneous development of malignancy in each breast occurred four times. In the other cases of this group the first lesion to appear was followed at various intervals by involvement of the other breast.

The coincidence of cancer of the breast and other types of cancer was noted in five patients. Two patients had cancer of the breast and cervix, while the association of mammary malignancy and basal cell growths situated on the face or scalp was noted three times.

Four patients had multiple cystic carcinomas (epithelioma adenoides cysticum). The areas involved were the face, scalp, neck, chest, arms and vulva.

Four patients presented malignant melanotic tumors, either multiple or associated with basal cell cancers.

One patient was found at operation to have four carcinomas of the stomach. Neither metastasis nor implantation from a single primary focus would explain all the malignant growths present.

In two patients more than two types of malignant neoplasms were observed. In one a basal cell epithelioma of the forehead, a sarcoma of the antrum, and bilateral adenocarcinomas of the breasts were noted. The other patient had malignant masses in each breast, in the mouth and on the cervix.

The author believes that many cases recorded as metastases or residual growth from neoplasms previously treated are not such, but are new foci of growth. A patient who has apparently been successfully treated for malignant

disease is not immune to further neoplastic lesions. In fact, the first growth may have indicated a susceptibility to malignant development, and for that reason patients who are under observation following the treatment of malignancies should be carefully observed for the appearance of new tumors, and should have all sources of local irritation removed, if that is possible.

MICHAEL, Houston, Texas.

THE ROENTGEN-RAY SHADOWS OF LUNG SYPHILIS AND SYPHILITIC TUBERCULOUS SYMBIOSIS IN THE LUNGS. W. WARNER WATKINS, *Am. J. Roentgenol.* **7**:259, 1921.

In terms of clinical pathology, one can distinguish three types of radiographic shadow produced by syphilitic invasion of the lungs: 1. The lesions of active or early syphilis produce shadows which are to be interpreted as (a) gummas, or (b) inflammatory consolidation or infiltration. Such shadows vary according to the virulence of the infection and the rapidity of the invasion. 2. The lesions of old, latent, or hereditary syphilis produce shadows which represent (a) interstitial peribronchial or peri-arterial fibrosis, or (b) dense fibrosis of the lung or pleura. 3. In conjunction with thoracic syphilis, indefinite lung densities occur, the nature of which has not yet been determined, either by clinical observation, pathologic research or radiographic characteristics.

Of patients radiographed for suspected lung or heart disease, 2.6 per cent., or 172 of 6,500 patients examined, had pulmonary shadows which could be reasonably considered as showing uncomplicated syphilis, although in many these shadows were associated with cardiac or aortic syphilis.

Of the 6,500 patients previously mentioned, 948 showed lesions of tuberculosis which had reached the advanced degree, according to the classification of the National Tuberculosis Association. In 209, or over 22 per cent. of the 948, a diagnosis of combined syphilis and tuberculosis was made.

Tuberculosis and syphilis may occur simultaneously in the same lung, each producing its own lesions, which can frequently be distinguished by the radiograph. The two diseases may also occur as a true symbiosis. The term symbiosis carries with it a tacit denial of the supposed antagonism between the organisms of tuberculosis and syphilis, for which there is no biologic or clinical evidence.

The importance of this symbiosis from a therapeutic standpoint is:

1. In the treatment of systemic syphilis, it is important to know whether the lungs are involved, since a Herxheimer reaction in the lungs may be serious.

2. It is doubly important in tuberculosis to ascertain whether the patient combats this comparatively benign single infection, or whether a sinister combination with active syphilis must be treated.

3. It may be triply important not to disturb the fibrotic changes of latent syphilis by arsenical treatment, if the tendency of this fibrosis is to arrest the tuberculosis.

GOODMAN, New York.

ON THE COLLOIDAL BENZOIN REACTION--GUILLAIN'S METHOD--IN THE SPINAL FLUID. ROQUE LÓPEZ, *Prensa Med. Argentina* **7**:286 (April) 1921.

Lopez describes a reaction introduced by Guillain, Laroche and Lechelle in France, which they think more accurate than Lange's gold test or the

Sachs-Georgi reaction. The technic is as follows: Six test tubes are placed in a rack and numbered from one to five, leaving the sixth as a control. In the first tube 0.25 c.c. of a 0.1 per cent. solution of sodium chlorid is placed; in the second, 0.5 c.c. of the same solution are placed; in the third, 1.5 c.c.; and in the fourth, fifth and sixth, 1 c.c. To the first three tubes, 0.75 c.c., 0.5 c.c. and 0.5 c.c. of spinal fluid, respectively, are added, the contents well mixed and then 1 c.c. of the mixture of tube number three is added to tube number four and 1 c.c. of the latter to tube number five. Tube number six contains no spinal fluid, being the control. One c.c. of the benzoïn colloidal suspension is then added to each of the six tubes, and the whole is left at room temperature until the next day when the test is read. The benzoïn suspension is prepared in the following manner: one grain of benzoïn is dissolved in 10 c.c. of pure alcohol; forty-eight hours later the supernatant fluid is decanted and three tenths of 1 c.c. are mixed with 20 c.c. of distilled water at 35 C.

All the glassware must be perfectly clean, the same precautions being taken as for the preparation of the colloidal gold fluid of Lange. On reading the test, if the fluid remains homogeneously cloudy, it is negative, but if the benzoïn is precipitated and the supernatant fluid appears clear, then the test is positive. The author has used this test in twelve cases with very satisfactory results.

PARDO-CASTELLO, Havana.

URTICARIA SYMMETRICA (DYSMENORRHOICA, MATZENAUER-POLLAND). C. KREIBICH, *Dermat. Wchnschr.* **71**:1043 (Dec.) 1920.

A girl, 24 years of age, had had attacks of red spots on the face since she was 9 or 10 years old and two attacks involving the whole body during the past year. These attacks were occasionally associated with tetany-like cramps in the hands. Menstruation began at the age of 22 and had occurred only five times in two years. Two types of skin changes were present: acute and chronic. The acute lesions consisted of hyperemic spots which persisted from six to twenty-four hours, leaving behind them a light cyanosis. They varied greatly day by day in size and shape, but were mostly symmetrically distributed over face, neck, arms and legs. Subjective symptoms consisted of burning; no itching was present.

The chronic changes consisted of areas of thickened skin, of a pigmented, dirty-grayish color which had a warty appearance in certain areas. In the axillae there was a papillary hypertrophy resembling acanthosis nigricans.

These thickenings seemed to be due to a piling up of the horny layer and could be partly removed with the fingernail. They were completely exfoliated when one of the acute erythematous patches formed under them. There was no weeping or crust formation associated with any of the lesions.

The acute lesions gave negative histologic findings; the chronic ones, a thickening of the horny layer with fingerlike projections of the papillae, a proliferation of the endothelial cells and a large number of mast cells in the cutis. No cells of acute inflammatory type were present.

Other findings in the patient were: hypoplasia of the inner and outer genital organs, beginning double cataract like that found in endocrine disturbances, medium enlargement of the sella turcica and poorly developed secondary sexual characteristics.

The disease corresponds to the hyperemias which the author has described (Die angioneurotische Entzündung, M. Perles) although the failure of the acute

hyperemic lesions to form hives and become necrotic is new. Another new variation is the secondary formation of papillary hyperplasia and hyperkeratosis due to repeated hyperemia.

KETRON, Baltimore.

THE CELLS OF LANGERHANS: THEIR RÔLE IN THE DERMO-EPIDERMIC EXCHANGES. P. MASSON (PAUTRIER), *Bull. soc. franç. de dermat. et syph.* **4**: R. S. 7, 1921.

To determine the physiologic function of these peculiar cells, which he considers to be of epidermic origin, the author has examined biopsy material from several cases, and he reports his findings in detail. In palpebral xanthelasma, in which the entire derma showed a cellular content high in lipoids and neutral fats, in the epidermis the cells of Langerhans also contained neutral fats and lipoids but practically no pigment. In a case of xanthoma the excess fat content was limited to the middle and lower derma, the papillae being nearly free; here the cells of Langerhans were found to contain no fat, although their pigment content was somewhat below par. In sections of radiodermatitis the content of certain epidermic cells and of certain cells of Langerhans corresponded to that of the subjacent connective tissue cells.

From these findings the author concludes:

1. The cells of Langerhans contain abnormal substances of the same order as those found in the cells of the papillae (e. g., fats or iron pigment). They contain little pigment when the dermic cells are loaded with fat; they contain little or no fat if the xanthomatous process does not extend up to the basal layer. Therefore they derive their normal content from the superficial dermic cells. Is this not the case in their normal metabolism?

2. The cells of Langerhans apparently contribute in turn to the content of the other epidermic cells, as is seen in the exchange of iron pigment.

3. They are therefore probably amboceptors between derma and epidermis.

4. Substances may be passed on directly from cell to cell through the derma and via the cells of Langerhans, to the epidermis. This may work both ways, in catabolism and in anabolism.

PARKHURST, New York.

PELLAGRA. W. J. MACNEAL, *Am. J. M. Sc.* **161**:469 (April) 1921.

This is a lengthy article dealing with the entire subject of pellagra, reviewing the work done and theories on the disease in recent years, especially with regard to the findings of the Thompson Pellagra Commission.

While the specific cause of pellagra is unknown, the writer believes the disease to depend on two factors—one of which is a living organism derived from a previous case of the disease, the other a factor or group of factors which reduce the resistance of the individual, among which he mentions malnutrition, cachexia of disease, overwork, climatic conditions, excessive child-bearing, old age, alcoholism, etc.

Pellagra exists when there has been a previous case of the disease, and the danger of contracting the disease increases with the proximity to the house of the pellagrin.

Some races appear to be more subject to pellagra than others but probably only in proportion to their racial resistance to disease, while it is most frequent in white women and children, older white men and negro women.

Certain dietary deficiencies are recognized as having a bearing on the production of the disease, but this is not confined to maize. Milk products and

fresh meat are the best foods for the prevention of pellagra. Poor sanitation is a factor in the spread of the disease, which up to the present has not been produced experimentally.

The article concludes with an excellent description of the symptomatology and pathology. Treatment is along the usual recognized lines.

JAMIESON, Detroit.

THE FILIFORM SPRAY IN DERMATOLOGY. VEYRIERES and FERREYROLLES, *Ann. de dermat. et syph.* **4**:156, 1921.

The authors have had pioneer experience in this field, and have found the treatment very beneficial in a number of conditions. Pruritus and lichenification, they say, readily succumb to it; pruritus vulvae, neurodermite, lichen planus and prurigo are mentioned as yielding favorably. Certain acnes, and especially rosacea, have been benefited, and telangiectases also, when the skin is sufficiently viable to resist the attendant trauma. It may be tried in cases of keloid and of scleroderma. In selected cases of lupus erythematosus and of lupus vulgaris it may be used as a curet, destroying the pathologic tissue and sparing the normal; the resulting scar is good.

The water, heated to the desired temperature, enters an airtight copper tank through a valved inlet. By means of a small electric pump a constant pressure of from 3 to 7 kg., as desired, is maintained within the tank; a relief valve is provided and also a gage to show the level of the water. There is also a thermometer and a pressure gage. Two exits are provided: a drain-cock and a pipe through which the water flows to the spray. At the end of a flexible rubber tube is a hard stone nozzle, pierced by a hole 0.5 mm. in diameter; through this opening the water flows, the nozzle being held at 20 to 25 cm. from the surface treated. The surface should be struck at right angles, the length of the application varying with the nature of the lesion. The optimum temperature is said to be about 33 C.

PARKHURST, New York.

SKIN DISEASES IN RELATION TO INTERNAL DISORDERS. JAMES GALLOWAY, *Lancet* **200**:364 (Feb. 19) 1921.

The author treats briefly of disorders whose causes are thought to be entirely external and local and on which health and disease exert influences by raising or depressing the powers of resistance and healing. Attention is then called to cutaneous manifestations, in many cases even more striking, but which must be regarded as phases or results of a general infective process or of some internal disorder. In discussing the action of alien protein, the author states that two facts stand out clearly for our recognition from the clinical point of view: 1. As the result of absorption of proteins alien to the invaded organism, eruptions make their appearance closely similar to the erythema group of skin diseases. 2. These eruptions vary in degree, severity and time of incidence, and these variations depend on stages of increased or diminished sensibility which may be acquired by artificial methods. Recognizing these salient points, we may see how large is the field of medical investigation which they indicate; moreover, they may serve to point out the path through a field of clinical medicine which is as yet little known.

WAUGH, Chicago.

A CASE OF HYPODERMIC SARCOID OF THE LEG. L. LAPLANE, *Bull. Soc. franç. de dermat. et syph.* **3**:75, 1921.

A woman of 51 years presented, just below the popliteal region, a flat plaque 16 cm. long and 2 cm. in depth, of a slightly purplish tint, quite firm and slightly tender on deep pressure. It had been present for seven years, but had grown considerably during the last year. On examination another nodule, the size of a small nut and violaceous, was found nearby. Tender lymph nodes were felt at the saphenous opening of that extremity; there was no genital or anal lesion to account for their presence. No popliteal adenopathy was found. Several typical patches of psoriasis, also said to be of seven years' duration, were present on the arms and legs; a mixed tumor of the parotid gland, diagnosed histologically, was found and excised. Other possibilities having been excluded, it was concluded that the tumor on the leg must be sarcoid. A biopsy was made and the sections were examined by Darier, who pronounced it a typical sarcoid of the Darier-Roussy type. A careful search revealed no tubercle bacilli. There was a definite history of tuberculosis in the immediate family, and the patient herself, with a strongly positive tuberculin reaction, gave a history of recent cough and night sweats; examination showed both apexes to be the seat of an apparently quiescent tuberculous process. The Wassermann reaction was strongly positive, though the history was not suggestive of syphilis.

For two months small doses of tuberculin were administered hypodermatically; then neo-arsphenamin was given and the tumor soon disappeared. As Darier says, this condition may be of tuberculous, syphilitic, lymphogranulomatous or other origin.

PARKHURST, New York.

WASSERMANN TEST WITH SECRETIONS, TRANSUDATES AND EXUDATES IN SYPHILIS, WITH A NOTE ON THE ORIGIN OF THE COMPLEMENT-FIXING ANTIBODY. J. V. KLAUDER and J. A. KOLMER, *J. A. M. A.* **76**:1635 (June 11) 1921.

The Wassermann reaction was positive three times in nineteen specimens of human milk; weakly positive in one instance among twenty specimens of saliva; moderately positive one time in thirty tests of seminal fluid; and doubtfully positive in ten specimens of aqueous fluid from the anterior chamber of the eye. Eleven specimens of exudates and transudates were examined with uniformly positive results.

The complement-fixing antibody in spinal fluid is regarded as being of dual origin, neural as well as hematogenous, while the Wassermann body in transudates and exudates is derived from the blood plasma.

The surface fluid from a number of chancres yielded almost uniformly ++++ reactions. Saline extracts from syphilitic testicular nodules in rabbits gave positive results. The authors suggest that this "local" Wassermann test may have a practical value in differentiating syphilitic from nonsyphilitic lesions, particularly when applied to chancre fluid as a means to the early diagnosis of syphilis.

MICHAEL, Houston, Texas.

PREROSEOLAR SYPHILITIC ICTERUS AND THE CLINICAL MANIFESTATIONS OF SYPHILIS PRECEDING THE ROSEOLA.

L. CHATELLIER and V. BONNETTERE, *Ann. de dermat. et syph.* **4**:165, 1921.

In a review of the literature the authors have found five cases of this early jaundice and they describe them, adding their own as the sixth. In their

own case and in one other, the icterus had appeared almost simultaneously with the chancre. Except in one case, of hematogenous jaundice, there were the classical symptoms of hepatic biliary obstruction, with the large tender liver, the pigmented urine and the clay-colored feces. The spleen was usually palpable. Itching was always absent. The temperature never exceeded 38 C. These symptoms disappeared, together with the chancre, under antisyphilitic treatment; in the authors' case there was also a coexisting albuminuria, which was quickly dispelled by the treatment.

As further evidences of the early generalization of syphilis, many other manifestations are cited, including periostitis, arthritis, phlebitis, carotid thrombosis (one case), splenomegaly, nephritis and a pruritic exanthem. The early advent of spirochetemia is mentioned and also the precocious meningeal and cranial nerve involvements. Therefore it is certainly evident that early syphilis does not reside in the chancre alone.

PARKHURST, New York.

FURTHER CONTRIBUTION TO THE STUDY OF ETIOLOGY OF EXFOLIATIVE DERMATITIS. KAREL HUBSCHMANN, *Ceska dermat.* 2:153 and 183, 1921.

The author reports two cases of secondary exfoliative dermatitis that showed evidence of hypothyroidism which probably was the main cause of skin disturbances. The first patient showed originally a vesiculo-urticarial affection, the second, an eczema. Under too vigorous a treatment the underlying vasoplegia, in all probability, became aggravated and led to the production of universal exfoliative dermatitis. As thyroidin helps to sustain the tonus of the skin capillaries, the patients were put on thyroid therapy. Both improved remarkably. The third patient presented a typical clinical picture of exfoliative dermatitis with the unusual history of short duration and an intense itching and burning, worse at night. A trichophytic basis being suspected, the patient was put on tar treatment (Rp. Picis lithanthracis, 5 gm.; benzoli, 10 gm.; acetoni, 35 gm.). He left the hospital completely cured in five weeks.

SPINKA, St. Louis.

STUDIES AND CONSIDERATIONS REGARDING THE BERLIN MICROSPORON EPIDEMIC. W. FISCHER, *Acta dermat.-ven.* 1:35, 1921.

Epidemiology, clinical aspects, parasitology and treatment are extensively considered by the author. This peculiar microsporon, which grows in abortive forms on ordinary mediums, first appeared in Germany in 1918; it attacked the children of Berlin and Hanover, spreading widely in the institutions. The patients were between 2 and 14 years of age and the ratio of boys to girls was 3:2. Both scalp and glabrous skin were attacked, a temporary depigmentation sometimes ensuing in the healed spots. The lesions were usually multiple and multifocal; patients with deeper lesions always reacted positively to an extract of mouse favus introduced intracutaneously, while a weakly positive reaction was given by 15 to 20 per cent. of those with superficial lesions.

The question of therapy is discussed at great length. Owing to technical difficulties, the roentgen-ray treatment proved a failure in many cases and was abandoned, arduous courses with strong irritants being substituted; from 5 to 20 per cent. of pyrogallol was the application of choice, and twenty weeks of this treatment were often necessary to bring about a cure. It was sometimes reinforced by roentgen-ray exposures. The importance of keeping the patients in institutions during treatment is emphasized.

PARKHURST, New York.

REGARDING DIFFERENT ASPECTS OF HEREDITY IN CASES OF
UNSUSPECTED ANCESTRAL SYPHILIS. J. AUDRAIN, Bull. Soc.
franç. de dermat. et syph. 3:85, 1921.

The author has observed thirty families, his records often reaching into the third and sometimes into the fourth generation. These findings are presented in detail, including not only the generally accepted stigmas of syphilis but also signs of various glandular (endocrine) alterations, which the author considers probably to be of the same origin.

As characteristics of syphilis he notes: (1) recurrent lesions in one organ or system, (2) functional hyperexcitability, that is, the "exaggerated ego," the great resistance to bodily discomfort, which the author has found common to these patients; this diminishes in succeeding generations. The less resistant endocrine glands are first attacked by the disease, and later the more resistant.

In congenital syphilis the paternal influence is the more marked, according to Audrain, and also more variable from year to year. The maternal influence, on the other hand, steadily decreases in its intensity, so that the prognosis from this standpoint improves with succeeding pregnancies. The offspring of two congenital syphilitic people are usually more severely attacked than was either parent.

PARKHURST, New York.

SUBACUTE MALIGNANT PEMPHIGUS WITH EXTENSIVE BULLAE.
L. BROcq, GOUGEROT, DESAUX and RABREAU, Bull. Soc. franç. de dermat.
et syph. 1:2, 1921.

A discussion of this condition appears in the *Ann. de dermat. et syph.*, serie 5, volume 7, and extracts from it are quoted here. The patient, a woman of 35 years, had enjoyed the best of health until April, 1920, when bullous lesions appeared about the mouth, involving the mucosa. The eruption spread until the first examination, made on Nov. 30, 1920, showed it to be generalized; the chest, back and lips were most severely affected, the lesions being confluent, while on the extremities they were scattered. The elementary lesion was a bulla with flaccid walls, with no attendant erythema; its contents were at first clear, but soon became cloudy. There was no pruritus. Rupture of the bullae revealed raw, weeping surfaces which were excessively tender. The bordering epidermis was progressively undermined, so that neighboring lesions became confluent. There was no tendency to healing. A slight fever accompanied the eruption, and in the two last months diarrhea and hematuria developed. Jan. 6, 1921, the lethal exitus occurred.

The bullae contained no bacteria, but a few eosinophil leukocytes. No satisfactory results were obtained in subsequent bacteriologic examinations, but it was thought that streptococci or the *Bacillus pyogenes* might have been causative.

PARKHURST, New York.

AN X-RAY BURN OF THIRD DEGREE FOLLOWED BY RAPID
HEALING. EDWARD S. BLAINE, Am. J. Roentgenol. 8:183, 1921.

A colored patient being treated for extensive blastomycosis of the pelvic region was inadvertently given a double exposure by an assistant. A complete tissue breakdown rapidly developed, and in eleven days the entire abdominal wall, the skin, subcutaneous and muscle tissues, in the exact areas treated, about 3 inches in diameter, had disappeared down to the peritoneum. The coils of intestines could be seen through the thin peritoneum which appeared as a more or less transparent veil. The patient did not complain

of much pain. No medication of any kind was given. In fifteen days the breakdown tissue had increased only slightly in extent. During the next few days a surprising change took place, and in one week one hardly recognized the area. The edges had filled apparently with regrown tissue, the hole had closed, and in thirty-nine days no definite evidence of the accident was visible. The remaining areas of revived blastomycotic growth were subsequently treated by roentgen-ray dosage of the same formula, and a complete cure was obtained. No untoward sequelae have occurred in three years, and the patient is now working.

GOODMAN, New York.

UNILATERAL CUTANEOUS INVOLVEMENT (THE TRUNK AND LOWER EXTREMITY) WITH PIGMENTATION, LEUKOMELANODERMA, INFILTRATION IN PATCHES; TROPHIC ULCERATIONS AND A ZOSTERIFORM DISTRIBUTION OF THE LESIONS. SPINA BIFIDA OCCULTA. L. QUEYRAT, A. LERI and RABUT, Bull. soc. franç. de dermat. et syph. 4:116, 1921.

A woman, 28 years of age, had first noticed the cutaneous manifestations in 1909, the calf being first involved. Fleeting paresthesias preceded and accompanied the involvement, which at first had a slate colored mottled appearance. It spread, including the thigh and the lower part of the trunk. There were trophic ulcers, first of the leg, then of the thigh. An examination revealed a spina bifida occulta of the eleventh and twelfth dorsal and the first lumbar vertebrae, in exact agreement with the distribution of the cutaneous lesions. The sacrum was also bifid, and there was considerable scoliosis.

Leri, the neurologist, reports three cases of spina bifida with trophedema, which may occur late in life; he speaks of pigmentation due to cord injuries. He and Darier are of the opinion that here we may have an explanation for some obscure cutaneous lesions. A fault in the nerve structures is the probable cause, rather than the vertebral discontinuity.

PARKHURST, New York.

ERYTHEMA CHRONICUM MIGRANS. A. AFZELIUS, Acta dermat.-ven. 1:120, 1921.

In a recent issue of *Acta Dermato-Venereologica* (3-4:422, 1920), Strandberg described a case under this name, a designation which was first suggested in 1908 by the author, Afzelius. Starting from a central papule, a narrow, scarcely elevated ring spreads peripherally, preserving its circular form for several weeks or even months, finally to disrupt and fade out. In many cases insect bites have been blamed, and the author thinks it likely that they are always causative. The pathology is thought to be that of a cellulitis rather than a lymphangitis, as has been alleged. It is in some ways analogous to Rosenbach's erysipeloid. Since it disappears without treatment, its diagnosis eliminates the necessity of disfigurement by strong applications or by surgery.

PARKHURST, New York.

TWO CASES OF LYMPHANGIOKERATOMA CIRCUMSCRIPTUM NAEVIFORME. FABRY and ZIEGENBEIN, Dermat. Wchnschr. 72:53 (Jan.) 1921.

The patient in Case 1 was a man 45 years of age, the disease had begun in childhood. The lesions were situated on the back and outer surfaces of the

lower portion of the right leg and ankle and consisted of groups of closely aggregated vesicles and raised nodular masses covered over grayish-white or grayish-violet warty, horny substance. The lesions had occurred after excision several years before.

Case 2 was that of a boy 9 years of age who had had the disease since birth. The lesions were situated on the dorsal and inner surfaces of the left foot and were similar to those in Case 1. The diagnosis was confirmed by histologic examination.

The author states that the association of hyperkeratosis with the circumscribed lymphangiomas has been noted previously only by Francis. He calls attention to the nevus-like distribution of the lesions in his cases.

KETRON, Baltimore.

LYMPHADENOMA OF THE VELUM PALATINUM ARISING FROM THE TONSIL. MILIAN, COTIENOT and MOUQUIN, *Bull. Soc. franç. de dermat. et syph.* **3**:71, 1921.

On July 17, 1920, a shoemaker appeared complaining of a painful ulceration of the left tonsillar region which had persisted for two years. A tonsillectomy had been of no help; the ulceration deeply invaded the posterior portion of the soft palate. Although the Wassermann reaction was repeatedly negative, the patient's wife had had two miscarriages, and the suggestive appearance of the ulcer prompted the administration of eleven neo-arsphenamin injections, totalling 5.85 gm. Healing promptly followed, but four months later the patient had to be hospitalized for a recurrence, this time for a shallower, though painful ulcer involving tissue adjacent to the scar of the former lesion. Again the Wassermann reaction was negative, and neo-arsphenamin was given with no benefit. While the blood picture and general physical findings did not suggest it, nevertheless a biopsy showed the ulcer to be typically lymphogranulomatous, and it responded readily to intensive cross-firing with the roentgen rays, only to recur once more fifteen days later. It was thought by some to be an "episyphilitic" phenomenon.

PARKHURST, New York.

THE INFLUENCE OF SYPHILIS ON THE PREGNANT WOMAN. GEORGE GELLHORN, *Surg. Gynec. & Obst.* **32**:535, 1921.

Gellhorn takes the attitude that the child has always had more consideration than the mother in syphilis in pregnancy. It appears that instead of running its usual course during pregnancy, syphilis is aggravated, and that many subjective symptoms of the disease are evident. Local manifestations, especially of the mucous membranes, are intensified. Primary lesions are said to be larger and more persistent. Condylomata lata increase in size and number, and the swelling of the glands makes rapid progress and not infrequently terminates in suppuration.

During labor syphilis in the mother may cause abnormal resistance of cervical tissues, or obstruction of the vaginal outlet. Malposition of the fetus may be due to syphilis because the fetus is either immature or macerated.

During the puerperium, the greatest danger lurks in infection because of retained membranes. Subinvolution may ensue.

Gellhorn's "practical conclusion is very obvious. Knowing that both mother and child are endangered, we must ever bear in mind the possibility of syphilis,

particularly when we have to deal with obscure recalcitrant disturbances in pregnancy, and once our diagnosis is made, we must give energetic and systematic treatment to such women throughout the period of pregnancy."

GOODMAN, New York.

A CONTRIBUTION TO THE STUDY OF THE ARSPHENAMINS; PEMPHIGUS FOLIACEUS FROM ARSPHENAMIN. J. NICOLAS and G. MASSIA, *Ann. de dermat. et syph.* **4**:145, 1921.

This rare complication develops rapidly after a few injections of arsphenamin, being ushered in by an erythematous papular or papulovesicular eruption. Its easily ruptured bullae, scales and flexural vegetations are those of ordinary pemphigus foliaceus, but there are no lesions of the mucosae, nails or scalp. Furthermore, the prognosis is good; there is complete recovery after a period of one or two months. Arsenical intoxication is possibly to blame, and we are warned to be cautious in the presence of the least erythema or flexural eczema.

The authors report three cases observed within the past five years. In two pruritus was present, in one there was a transient nephritis, and in one gangrene of the foot occurred with a fatal outcome.

PARKHURST, New York.

ROENTGEN-RAY TREATMENT OF CUTANEOUS CANCER. H. H. HAZEN, *J. A. M. A.* **76**:1222 (April 30) 1921.

Hazen reports experiences in the roentgen-ray treatment of the various forms of cutaneous cancer.

Basal-Cell Cancer.—The large majority of patients were treated by measured dosage, using an interrupterless transformer and Coolidge tube. The dose was approximately 2 skin units, unfiltered in most instances. When deep infiltration was present, filtration through 1 mm. of aluminum was used. Most patients required at least three treatments to effect a cure; a few received from four to many.

RESULTS OF TREATMENT

	No. of Cases
Well 3 years.....	16
Well 2 years.....	17
Well 1 year.....	39
	<hr/>
Relapses cured	4
Relapses healed	2
*Healed	41
	<hr/>
Not cured	119
	<hr/>
	16

*Healed represents clinically cured cases that have been followed for less than one year.

It should be noted that epitheliomas involving the cartilage of the ear or eyelid are particularly resistant to this form of therapy. Intractability of cancers involving cartilage is probably due to the failure of cellular reaction in the invaded tissue.

There were eleven relapses in this series of basal cell growths. All relapses developed within the first year after treatment.

Prickle-Cell Cancer.—Fifteen patients with this type of growth were treated. Four were permanently cured; the lesions of three healed under treatment

(time too short since treatment to determine end-results); and eight were not in the slightest degree influenced.

Miscellaneous Growths.—Failure is reported in one case of rapidly growing sarcoma. In a patient with a malignant mole of the temple. The original growth was destroyed by one intensive treatment, but a year later metastases appeared and the patient speedily succumbed. A child with xeroderma pigmentosum was relieved of lesion after lesion for two years, but died at 4 years of age from the disease.

MICHAEL, Houston, Texas.

SYPHILIS-CARCINOMA. J. STRANDBERG, *Acta dermat.-ven.* **1**:8, 1921.

The author reports three cases of fatal epithelioma arising apparently on gummatous ground, two on the penis and one on the tongue. The patients were men about 60 years of age; two presented multiple cutaneous foci of syphilis. In none of the carcinomas were signs of syphilis found histologically, but this was perhaps due to the recent antispecific treatment.

Syphilis-carcinoma is compared with the much more common lupus-carcinoma, alleged causes for the frequency of the latter being its greater chronicity and its more marked tendency to epithelial proliferation. The rapid course of both is attributed to the lessened resistance of tissues already diseased.

Early diagnosis, though often wellnigh impossible without a biopsy, offers the only hope of saving the patient.

PARKHURST, New York.

PREVENTION OF ACUTE ARSPHENAMIN REACTIONS BY ANTI-ANAPHYLAXIS AND ATROPIN. G. J. BUSMAN, *J. A. M. A.* **76**:1302 (May 7) 1921.

Busman declares that practically all patients who exhibit an idiosyncrasy to arsphenamin as shown by the development of acute nitritoid reactions or late gastro-intestinal upsets may be protected by preliminary administration of atropin or the production of anti-anaphylaxis, or a combination of both measures.

If atropin is used alone, it is given in one dose of $\frac{1}{50}$ grain twenty minutes before the injection of arsphenamin. The author's observations confirm those of Stokes as to the value of this drug.

The production of anti-anaphylaxis is accomplished by injecting a "vaccinating" dose (one tenth of the total dose) one hour before the subsequent larger portion is given.

In many patients, one or the other of these measures may suffice, but in highly sensitive patients the conjoint use of both methods is indicated. Under these circumstances the preliminary injection of one tenth of the total dose of arsphenamin is given, followed in twenty minutes by $\frac{1}{50}$ grain of atropin, and twenty minutes later the remaining portion of arsphenamin is administered. The use of these methods has practically eliminated the reaction in susceptible patients and has made possible the continuance of treatment when repeated; severe reactions would otherwise have forced its abandonment.

MICHAEL, Houston, Texas.

STUDIES OF THE STABILITY OF BLOOD SUSPENSIONS IN SYPHILITIC PATIENTS UNDER TREATMENT. K. HEDEN, *Acta dermat.-ven.* **1**:74, 1921.

It has been found that in many febrile diseases, in pregnancy and in florid secondary syphilis blood corpuscles are deposited from a citrated blood more

rapidly than in normal persons. Similar changes have been found in other syphilitic conditions, including late neurosyphilis and arteriosclerosis. This may be due to changes in the hydrogen-ion concentration of the blood.

In a series of eighty-six patients, the author has found that the administration of colloidal mercury and mercurial (gray) oil hastens sedimentation in a large percentage of cases, the former causing more alteration than the latter. This is thought to be a danger signal. Anemia is an important cause of quick sedimentation, and should be ruled out by a blood count in each case. In active syphilis a too rapid sedimentation may be remedied by treating the disease. Arsphenamin, unlike mercury, does not seem to produce instability of the blood suspension.

PARKHURST, New York.

THE SPIROCHETICIDAL VALUE OF DISODIUM ETHYL ARSINATE (MON-ARSONE). H. J. NICHOLS, J. A. M. A. **76**:1335 (May 14) 1921.

The claims made for the therapeutic efficiency of this drug, as well as requests for information on this point, led Nichols to investigate its effect on *Spirochaeta pallida* and experimental lesions. Rabbits were used exclusively in the investigation.

The experiments showed the minimum lethal dose of monarsonate may be taken as 0.075 gm. per kilogram. The corresponding fatal dose for a 70 kg. adult would be 5.25 gm. The dose of 2 gm. which is advocated, is, therefore, closer to the theoretically dangerous point than is considered safe with other arsenicals.

The minimum effective dose was found to be 0.33 gm. Comparison of this result with that determined as the minimum lethal dose shows that the drug has as much or more poisonous effect on the tissues as on the spirochetes. For its practical use in syphilis there is no such germicidal basis as exists in case of the arsphenamin group.

Nichols quotes Voegtlin and Smith as finding for both sodium cacodylate and ethyl arsiniate a ratio of minimum lethal dose: minimum effective dose of 1, while the same ratio for neo-arsphenamin was 28, and for arsphenamin 17. These investigators used trypanosomes as test organisms.

MICHAEL, Houston, Texas.

A VERRUCOUS AND HYPERKERATOTIC FORM OF MYCOSIS FUNGOIDES IN THE PREFUNGOID STAGE. E. JEANSELME and M. BLOCH, Bull. soc. franç. de dermat. et syph. **4**:110, 1921.

This unusual manifestation was presented by a woman, 35 years of age. In 1914 she had noticed the presence of three nonpruritic erythematous patches which remained for a month and disappeared with the advent of pregnancy. Three years later a new and similar eruption appeared, with a moderate pruritis; this time it persisted, involving the skin of all regions but sparing the mucous surfaces. There was slight malaise and loss of weight. A moderate leukocytosis was present, with a 6 per cent. eosinophilia; there was anemia with a high color index; firm, discrete lymph nodes were palpable in the groins and axillae. Sections from a biopsy showed the characteristic picture of mycosis fungoides.

Roentgen-ray treatment dispelled the lesions, leaving only pigmented spots, slightly infiltrated in places.

PARKHURST, New York.

CONGENITAL SYPHILIS OF THE SECOND GENERATION. MILIAN and VALLE, Bull. Soc. franç. de dermat. et syph. 4:114, 1921.

A boy of 7 years, whose nose and palate were the site of extensive destruction, presented unmistakable signs of the congenital affection, such as interstitial keratitis, rhagades, prominent frontal bossae and sluggish mental development, in addition to a strongly positive Wassermann reaction. The father had been killed at war; he had shown no signs of syphilis. The mother, however, presented stigmas of congenital syphilis, a perforation of the palate and a saddle-nose. She had had no miscarriages. The maternal grandfather had long been tabetic.

Jeanselme and Simon, in the discussion, each mention a case of this transmission in which the father was apparently free from the disease. Apropos of the similarity of the lesions in mother and child, Pinard recalls such a case which was reported by Queyrat in 1906.

PARKHURST, New York.

HEREDOLUETIC DISEASES OF CENTRAL NERVOUS SYSTEM IN CHILDHOOD. O. TEYSCHL, Ceska Dermat. 2:177, 1921

The author reports several cases of congenital syphilis of cerebrospinal type in children. He advises an examination of blood and spinal fluid in all nervous affections in children, no matter what the anamnesis is, as in all cases a syphilitic basis could be determined. He considers the usual dose of arsenphenamin as recommended by Peritz (0.01 gm. per 1 kg. of body weight) too high and advises an individual modification. He believes it advisable to put a new-born child of syphilitic parents immediately on an antisyphilitic treatment, whether the child bears signs of syphilis or not.

SPINKA, St. Louis.

THE SKIN AND ITS REACTIONS. ARTHUR J. HALL, Lancet 20:426 (Feb. 26) 1921.

The author considers the following points in the relation of skin diseases to internal disorders: 1. The skin is not merely a covering, but itself an important organ. 2. Its duties relate chiefly to events occurring outside the body. 3. While some of these reactions are local processes in the skin, the majority of them are controlled and regulated by the central nervous system and are in the nature of reflex actions. 4. Like all other reflex actions, they are capable of excitation from places other than the outside and of being modified by the condition of the central nervous system resulting from changes in the internal organs. In this sense, they must depend on the body as a whole at any given time. The author believes that many changes in the skin now attributed to internal disorders are capable of explanation as natural reactions of the skin to definite stimuli. Emphasis is placed on personal idiosyncrasy to certain irritants with a record of an interesting case.

WAUGH, Chicago.

A CLINICAL, EXPERIMENTAL AND PARASITOLOGIC STUDY OF THE ERUPTION IN MAN PROVOKED BY THE SARCOPTIC ITCH OF THE CAT. G. THIBIERGE and J. STIASSNIE, Bull. Soc. franç. de dermat. et syph. 1:17, 1921.

Thibierge described this eruption in the *Gazette des Hopitaux*, Jan. 31, 1911, and this is a report of further observations, with reference to several cases.

The eruption may involve only the part of the body which has been in contact with the cat, such as the chest or the shoulder, or, if contact has been prolonged, it may be extensive and even generalized. The element is a small papulovesicle on a wheal-like base; soon excoriated, it becomes crusted at the center, bearing some resemblance to a prurigo papule. Their appearance in successive crops gives the whole a polymorphous appearance which is misleading. There is nothing characteristic about the eruptive element, so that the diagnosis is difficult unless this possibility is kept in mind.

The causative parasite is present in the skin for twenty-four hours after contact with the infected cat, and it can occasionally be found in the lesions. It is the *sarcoptes minor*. This eruption is comparable to those arising from horse mange and from *pediculoides ventricosus*.

PARKHURST, New York.

THE INFLUENCE OF LUMBAR PUNCTURE ON SYPHILITIC ERUPTION. KARL SCHREINER, *Wien. klin. Wchnschr.* **34**:264, 1921.

It has often been noted during the last year that patients in the secondary eruptive stage of syphilis have shown marked improvement in lesions even with no treatment if lumbar puncture has been performed. Pustular eruptions seem to be influenced best, but moist, even condylomatous, lesions have shown a change for the better. Although no definite records are given, it is stated that on several occasions when more than the ordinary amount of fluid was withdrawn, the improvement was more marked. On the other hand, several failures to withdraw fluid were accompanied by clinical improvement, and it was thought that the preliminary epinephrin-cocain anesthesia may have been the cause of the change. Several patients, nonsyphilitic, were treated by injections of epinephrin. Scrotal eczema showed startling improvement with this treatment alone; there was less marked improvement in a case of varicose ulcer and in a case of scrotal eczema.

GOODMAN, New York.

ANAPHYLACTIC URTICARIA. G. PIGNET, *Ann. de dermat. et syph.* **4**:184, 1921.

In a tuberculous patient the nineteenth injection of a calcium-potassium-manganese compound produced a fleeting urticaria and malaise; the twentieth, three days later, was followed by a more pronounced systemic reaction and a rather severe urticaria of 48 hours' duration. The injections were discontinued for three months and then renewed, 1 mg. of epinephrin having first been given. An erythema immediately developed along the course of the veins used for the previous injections, although this time the opposite arm was used. This local erythema soon became a large urticarial wheal. It may have been that the walls of these veins were still impregnated with the manganese salts, but no positive explanation of the reaction could be offered.

PARKHURST, New York.

PAPULONECROTIC TUBERCULIDS OF THE FACE (ACNITIS).

MILIAN and THIBAUT, *Bull. soc. franç. de dermat. et syph.* **4**:112, 1921.

A woman, 31 years of age, presented the characteristic lesions of Barthelemy on the forehead, eyelids and nasolabial regions, and on the sides of the neck. She said they had been present for six months. A concomitant syphilitic infec-

tion had been treated without the slightest alteration in the facial lesions, and their true nature was subsequently shown by histologic examination. The physical examination revealed signs of apical pulmonary involvement, supposedly tuberculous. The patient had never menstruated.

PARKHURST, New York.

SYPHILITIC IRITIS: ITS RACIAL INCIDENCE AND ITS ASSOCIATION WITH SECONDARY SYPHILIS AND WITH NEUROSYPHILIS. F. L. ZIMMERMANN, J. A. M. A. **76**:1818 (June 25) 1921.

Among 228 white patients with secondary syphilis in the Johns Hopkins Clinic, there were four, or 1.76 per cent., with acute iritis; among 279 negroes, iritis occurred in thirty-six, or 12.9 per cent.

The incidence of iritis in all types of syphilis was 1.1 per cent. for white, and 3.2 per cent. for negro patients.

In the negro, iritis occurs in 10 per cent. of all cases of secondary syphilis, with a great predilection (approximately 33 per cent.) for the follicular papular syphilid.

The incidence of cerebrospinal abnormalities was not greater in partially treated patients with iritis than in the fluids of treated patients who had not had iritis.

MICHAEL, Houston, Texas.

A COMPARISON OF THE ACTION OF MERCURY ON THE BODY WEIGHT WITH THAT OF ARSPHENAMIN. J. ALMKVIST, *Acta dermat.-ven.* **1**:91, 1921.

In general the author found that arsphenamin increased the body's weight while mercury caused a diminution. This was repeatedly shown in a series of cases, with exceptions of course. It was often found that when the two treatments were given in alternate courses, the weight of the patient would vary accordingly. Interesting tables are given, and the discussion is exhaustive, with a long bibliography.

The moral is: When the patient loses weight under treatment, endeavor first to stop the loss by hygienic measures, both oral and general, and by stimulating the appetite; failing in this, the dosage of mercury must be reduced.

PARKHURST, New York.

A SYPHILITIC CHANCRE OF THE VAGINA. H. BREIDE, *Acta dermat.-ven.* **1**:114, 1921.

Perhaps because they are easily overlooked, vaginal chancres are thought to be rare, relatively few having been reported. It is possible that the structure of the vaginal wall and its secretions may discourage infection.

A girl of 20 years, with a typical early secondary eruption that involved the skin but not the mucosae, presented a typical sclerosis of the right vaginal wall 2 cm. below the cervix. There was no inguinal adenopathy; no spirochetes were found. The Wassermann reaction was found to be positive, and all the manifestations soon disappeared under antisyphilitic treatment.

The literature on the subject is briefly reviewed.

PARKHURST, New York

SYPHILIS IN CHILDREN OF SCHOOL AGE. B. F. DONALDSON, New York
J. Med. **21**:176 (May) 1921.

Of 28,000 school children, 167 were found to show evidence of organic heart disease, and among these there were thirteen cases of aortic insufficiency. Eighty-four of the children were selected for special observation, and 103 Wassermann reactions were performed on these and on the mothers and available relations of children with aortic insufficiency. A positive Wassermann reaction was obtained in only one child, a compensated case of aortic insufficiency, apparently in good health, with a history of tonsillitis and one attack of rheumatism. The mother's Wassermann reaction was + + + +. The patients with aortic cases all had definite histories of acute rheumatic fever, except one who had only diphtheria.

WILLIAMS, New York.

CUTANEOUS PIGMENTATIONS FOLLOWING SECONDARY SYPHILIDS. G. THIBIERGE and J. STIASSNIE, Bull. Soc. franç. de dermat. et syph. **3**:70, 1921.

This case was shown to emphasize the fact that pigmented spots may remain in the sites of faded secondary syphilodermas. A servant girl, aged 23 years, who had just recovered from rather severe secondary manifestations, presented such pigmentation about the neck in spots in which papulosquamous lesions had faded. They were configurate in places, especially at the front and sides of the neck.

According to Darier, the pigment in these lesions is located equally in the papillae and in the epidermis. By way of treatment, Balzer recommends the use of 5 per cent. white precipitate ointment, which has given good results in his experience.

PARKHURST, New York.

MYELOPLAXOMA OF THE TONGUE. V. ALOI, Riforma med. **37**:219 (March) 1921.

Sarcoma of the tongue is rare. The case reported by Aloï commenced one year before on the right side of the tongue as a small ulcerating lesion which the patient thought due to trauma. A tumor developed from this ulcer, and, growing very rapidly, invaded the whole organ forming an edematous, red mass which prevented the closing of the mouth and made speech impossible. The tumor was very painful, and the patient lost weight and rapidly became cachectic. Microscopically the diagnosis was sarcoma (myeloplaxoma). The author thinks that the origin of this tumor was in all probability in an embryonic nucleus of periostic tissue abnormally included in the tongue.

PARDO-CASTELLO, Havana.

A CASE OF URTICARIA PIGMENTOSA. MILIAN and PERIN, Bull. soc. franç. de dermat. et syph. **4**:126, 1921.

Occurring in a woman 58 years of age, in whom it had persisted since her 38th year, this eruption was doubly interesting because of its late appearance and its chronicity. Furthermore, there was a concomitant glycosuria, suggesting the possibility of hepatic trouble, which may play a part in the etiology of urticaria pigmentosa as it often does in xanthoma. The existence of syphilis invited speculation as to whether the hepatic and cutaneous alterations might not both be of specific origin.

PARKHURST, New York.

A CASE OF LYMPHANGIOMA OF THE BUTTOCK. G. THIBIERGE and P. LEGRAIN, *Bull. soc. franç. de dermat. et syph.* **4**:128, 1921.

A girl of 27 years presented a typical superficial lymphangioma of verrucous and vesicular appearance, present since birth, but which had not grown perceptibly until the tenth year. When last examined it was 12 cm. long and 7 cm. wide. Histologically there was found a surrounding area of fibrosis, deprived of elastic tissue, an inflammatory small lymphocytic infiltration and a perivascular plasmoma.

PARKHURST, New York.

THE HISTOLOGIC STRUCTURE OF HEMOLYMPHANGIOMA. HUDELO and CAILLIAU, *Bull. soc. franç. de dermat. et syph.* **4**:130, 1921.

This case had been presented at the last meeting of the Society, and the lesion had since been excised, sectioned and studied in detail. Both the subpapillary and the subdermal blood and lymph vessels were found to be involved, and there was considerable degree of connective tissue and muscular atrophy; the sudoriparous and sebaceous glands were also hampered.

A detailed report is given, with two illustrations.

PARKHURST, New York.

PHOTOTHERAPY IN BENIGN DISEASES OF THE SKIN. HERBERT F. PITCHER, *Am. J. Electrotherap. & Radiol.* **39**:143 (April) 1921.

This clinical paper dealing with the more common applications of the roentgen ray and ultraviolet ray in dermatology in which the static brush discharge and the vacuum and nonvacuum high frequency electrodes are advocated as auxiliary measures. The author claims that he obtained excellent results in the treatment of lupus erythematosus by using the water-cooled quartz-mercury vapor lamp with compression to cause ischemia, in exposures of from five to thirty minutes' duration, at weekly intervals, during a period of from three months to two years.

H. R. FOERSTER, Milwaukee.

TERTIARY SYPHILIDS OF THE FACE RESEMBLING LUPUS VULGARIS, REMARKABLY CONFLUENT. PAUTRIER, *Bull. Soc. franç. de dermat. et syph.* **4**: R. S. 13, 1921.

The patient, 40 years of age, was the mother of six children, five of whom were living and well. The cutaneous lesions, of two and a half years' duration, had first appeared on the chest, later involving the arms, face and scalp. There were many soft brown nodules, similar to those found in lupus vulgaris, but the gyrate arrangement of the lesions on the arms, the history of a very short duration, and the positive Bordet-Wassermann reaction all spoke in favor of syphilis. Within six weeks the patient received 4.2 gm. of neo-arsphenamin and seven injections of calomel; there was marked improvement in the lesions.

PARKHURST, New York.

A SYPHILITIC SCLEROGUMMATOUS INFILTRATION OF THE TYPE OF HYPODERMIC SARCOID. BURNIER and M. BLOCH, *Bull. soc. franç. de dermat. et syph.* **4**:136, 1921.

A deep, nonulcerating infiltration of the calf was presented by a man, aged 38 years, who had had a chancre twenty-two years previously. The tumor had been present for eighteen months, and had finally attained a length of

13 cm. and a width of 6 cm. The muscles of the leg were involved. A biopsy was performed, and the sections showed the typical structure of hypodermic sarcoid. After eight days of treatment with mercury cyanid and potassium iodid, the infiltration had diminished one third. The tuberculin reaction had been negative, and syphilis must here be considered as an etiologic factor.

PARKHURST, New York.

STUDY OF THE ACTION OF CERTAIN DRUGS ON SYPHILIS. M. COPELLI, *Gior ital. d. mal. ven.* **67**:24, 1921.

There are certain drugs, besides arsenic, mercury and iodine, which experimentally exert a favorable influence on syphilitic lesions. These are vanadium, phosphorus and antimony. Vanadium and antimony, especially, have shown, according to the author's observations, remarkable antisyphilitic properties. Two or more of these drugs united in a chemical compound seem to be more active. A preparation of arsenic, vanadium, phosphorus and antimony with a molecule of an organic acid (nucleinic) has proved to be highly parasitotropic without any toxic action on the cells of the host. This compound is therefore a valuable spirocheticide.

PARDO-CASTELLO, Havana.

A DISSERTATION UPON CARBUNCLES. SIDNEY PHILLIPS, *Lancet* **200**: (Jan.) 1921.

The author quotes the opinions of many authorities in regard to their views of a carbuncle. Some regard a carbuncle as an affection of the skin only, others as an affection of the skin and subcutaneous tissue, while others do not believe the skin is involved at all. Phillips believes that it is a gangrene of deep skin or deeper tissues due to a local invasion of pyogenic bacteria. The author discusses the cause of sloughing, the pathology, symptoms and types of carbuncles, also diagnosis and treatment. The article is lengthy and covers the subject thoroughly. Nothing new of importance is suggested regarding treatment.

WAUGH, Chicago.

MULTIPLE EXTRAGENITAL SYPHILITIC CHANCRES. H. ENGELSON, *Acta dermat.-ven.* **1**:69, 1921.

Two cases are reported: that of a girl of 22 years with a chancre on each lip, and that of a girl, aged 24, with a lesion on each tonsil. In the second case spirochetes were found, their absence on examination in the first case being attributed to the recent use of strong antiseptics. In each there was a clear-cut history of infection by the kisses of a syphilitic lover. The lesions soon disappeared under antisyphilitic treatment, but the second patient unfortunately acquired a generalized desquamative arsphenamin eruption which lasted four months.

PARKHURST, New York.

RAYNAUD'S SYNDROME WITH GANGRENE, FOLLOWING NEO-ARSPHENAMIN. J. NICOLAS, G. MASSIA and D. DUPASQUIER, *Ann. de dermat. et syph.* **5**:193, 1921.

A Swiss mechanic, 28 years of age, who probably did not have syphilis, had nevertheless received several small neo-arsphenamin injections. After the first and each succeeding injection, there were paroxysms of acrodynia with

acrocyanosis, at first fleeting but later persistent, the fingers, toes, tip of the nose and ears being affected. After three months gangrene ensued, with loss of the finger-tips. As there had been no sign of the affection before the arsenical was given, neo-arsphenamin is blamed.

PARKHURST, New York.

TWO CASES OF PIEDRA. L. PAIS, *Riforma med.* **37**:266 (March) 1921.

Two cases of this rare disease of the hair are reported. The nodules in both cases were made up of spores closely aggregated. The cultures identified the fungus as the *Trichosporum beigeli*. Intravenous injections of the cultures in rabbits and skin inoculations in human beings gave negative results. The author concludes that the *Trichosporum beigeli* has no pathogenic properties, but lives as a saprophyte on the hair.

PARDO-CASTELLO, Havana.

THE FILIFORM DOUCHE IN DERMATOLOGY. A. DESAUX and NOEL, *Ann. de dermat. et syph.* **5**:218, 1921.

A description of this apparatus has been previously given in a similar article by Veyrieres and Ferreyrolles, which appeared in the *Annales* (**4**:156, 1921) and has been abstracted. The general scheme of treatment recommended is given in the following table:

Lesion	Temperature of water	Pressure of Water	Diameter of Jet	Duration of Application
Acne	38-40 C.	5-7 atm.	½-1 mm.	Variable
Rosacea	35-38 C.	5 atm.	½-1 mm.	5-10 min.
Acne and rosacea.....	38-40 C.	5-6 atm.	½ mm.	Variable
Facial folliculitis	40 C.	3-7 atm.	½ mm.	Variable
Neurodermite	38-40 C.	5-8 atm.	½-1 mm.	Variable
Old lichen planus.....	40 C.	6-8 atm.	½ mm.	Variable
Facial verrucae planae*.....	35-38 C.	4 atm.	½ mm.	Brief
Lupus vulgaris*.....	35 C.	6-7 atm.	½ mm.	Long and thorough
Fixed lupus erythematosus*..	40 C.	6-7 atm.	¼-½ mm.	5-6 min., thorough

* Not superior to other modes of treatment here.

In all except lupus vulgaris the treatments may be repeated, and parts of extensive lesions are treated at different sittings. Healing is prompt and scarring slight. In lupus vulgaris auxiliary measures may be needed, such as the curet or the cautery. Anesthesia is usually unnecessary, except in the treatment of lupus.

This subject will be dealt with more fully in a future paper.

PARKHURST, New York.

TINEA OF THE BEARD CURED RAPIDLY BY INTRAVENOUS INJECTIONS OF GRAM'S SOLUTION. P. RAVAUT, *Ann. de dermat. et syph.* **5**:229, 1921.

Other treatments having been of no avail, a stubborn case of nearly four months' duration was soon cured by twelve intravenous injections of Gram's solution, given every other day, in doses increasing from 1 to 5 cm., diluted in water. Although the use of external treatment is ordinarily simpler, this result is considered interesting in view of the exercise of internal influences, such as the hormone changes at puberty or the changes effected in this case, in bringing about a cure.

PARKHURST, New York.

CONGENITAL SYPHILIS AMONG THE NEWLY BORN. S. M. ROSS
and A. F. WRIGHT, *Lancet* **200**:321 (Feb. 12) 1921.

This article contains an interesting report of an investigation by the authors to determine the presence of congenital syphilis in unsuspected cases. The blood was secured at birth from the placental end of the umbilical cord, part of the specimen being sent to each laboratory. The authors state that the number of specimens (284) are too small from which to draw any definite conclusions, but the results obtained were significant and warrant further investigation, since 3.5 per cent. were found positive by both observers using entirely different methods in different laboratories.

WAUGH, Chicago.

EXPERIMENTAL CHANCROID IN THE MONKEY AND THE RABBIT.
J. REENSTIERNA, *Acta dermat.-ven.* **1**:1, 1921.

In a monkey (*Macacus rhesus*), at the site of inoculation with pure cultures of the streptobacillus chancroids developed clinically typical in appearance. The streptobacillus was obtained from the pus, and it was also demonstrated in sections from the lesions. Its inoculation into the author's arm gave rise to typical chancroids, from which were obtained the organisms in pure culture.

Scrotal inoculations produced typical lesions in four of ten rabbits. Streptobacilli were recovered and produced chancroids on the arm of the author, which in turn yielded the organism in pure culture.

Similar inoculations into ten guinea-pigs, ten white mice, one rabbit, one goat and four sheep gave completely negative results.

The cutaneous reaction of Ito (with streptobacillus vaccine) on the author's arm ten months after these inoculations gave a strongly positive result.

PARKHURST, New York.

MEDICAMENTS NEW AND OLD. O. MICHAELIS, *Acta dermat.-ven.* **1**:
23, 1921.

In essence this article is a discussion of the advantages and disadvantages of sulfarsenol (a proprietary arsphenamin preparation), which may be summarized as follows: In the treatment of syphilis it is not superior to neo-arsphenamin. It is said to be of value in the control of certain complications of gonorrhea; this the author discusses at some length.

PARKHURST, New York.

CAN SPIROCHETES CAUSE PSORIASIS? P. SAVNIK, *Ceska Dermat.*
2:161, 1921.

The author reviews the literature on the subject and reports the results of his personal investigations. He does not consider the cocci and spirilla found in psoriatic scales as etiologically significant; such can be found in other skin diseases and even in a normal skin. He has not found the spirochete "sporogona psoriasis" of other authors in any of his specimens. On several occasions, however, he did notice the presence of small, round, actively motile, shiny bodies, forming chains of 2, 3, 5 and 8 individuals and joined by a fine dull filament.

SPINKA, St. Louis.

NOTES ON MONGOLISM. HUGH THURSFIELD, Brit. J. Child. Dis. **205-207**:18 (Jan.-March) 1921.

These notes concern forty-two mongol children seen by the author between 1912 and 1916. He could not attribute the condition to syphilis or tuberculosis. Some of the accompanying defects are briefly considered. The fissured tongue, so pronounced and characteristic in older mongols, is not present for the first few months of life. The author has seen it as early as the twelfth month, but it is not usually a striking peculiarity until after dentition has advanced, in the second year. By the fifth year it is generally marked. There was also noted scantiness of hair, a scurvy skin, and a tendency to catarrhal conditions of the upper respiratory tract.

PARKHURST, New York.

A CASE OF MULTIPLE LEIOMYOMAS OF THE SKIN. BURNIER and M. BLOCH, Bull. Soc. franç. de dermat. et syph. **1**:24, 1921.

The patient was a man, aged 43 years, who had first noticed the condition eight years previously. At that time a nodule appeared on the neck, and three years later more of them developed on the trunk, forearm and leg. These tumors were pea- to lentil-sized, brownish-yellow, firm and at times tender and even painful. A histologic study showed the growth to consist of bundles of smooth muscle fibers, not walled off from the surrounding tissues. A few lymphocytes, plasma cells and mast cells were found. The tumors disappeared under bipolar electrolytic treatment. Darier remarks that in these cases radiotherapy is useless.

PARKHURST, New York.

LATENT SYPHILIS IN A MEDICAL DEPARTMENT. E. HESS THAYSEN, Lancet **200**:213 (Jan. 29) 1921.

The author discusses the frequency of positive Wassermann reactions in medical cases with, and in the absence of, a syphilitic history and advises the test as a routine measure. The diagnostic value of the Wassermann test is considered carefully, and the difficulty as well as the danger of basing a diagnosis on a positive Wassermann reaction in the absence of clinical findings is admitted. The article is very interesting and should be read in its entirety by those interested in the subject.

WAUGH, Chicago.

A CASE OF SYPHILITIC REINFECTION. E. JEANSELME and ALTHABEGOITY, Bull. Soc. franç. de dermat. et syph. **1**:10, 1921.

The authors urge that all cases of suspected reinfection be scrutinized thoroughly before presentation, so that only bona fide cases may go on record. Theirs presented the following points: 1. The second chancre was in a different site from the first. 2. It was erosive, not ulcerated. 3. It contained abundant *Spirochaetae pallidae*. 4. The patient had been thoroughly treated for four years after the first attack. At the time of the occurrence of the second chancre the blood and the spinal fluid were examined and found normal.

PARKHURST, New York.

A CHRONIC RELAPSING BULLOUS AND PUSTULAR ACRODERMATITIS. HUDELO and PICARD, Bull. Soc. franç. de dermat. et syph. **1**:12, 1921.

A boy of 11 years had been afflicted since he was 2 years old, each outbreak being preceded by general malaise and vague paresthesias. The hands

and feet were especially involved, there being a painless paronychia and extensive nail deformity. The arms, legs and face also showed lesions, the bullae being surrounded by erythematous halos, and of short duration, the pustules being small, intensely inflammatory and more persistent. One of several Wassermann reactions was positive, and antisyphilitic treatment was administered. Locally, various antiseptic dressings were applied, and finally endocrine therapy (thyroid and suprarenal) with roentgen rays and high frequency treatment, but the attacks continued almost as severely as before. This may have been a case of erythema multiforme, although the blood showed no eosinophilia, or the syphilis may have been a determining factor.

PARKHURST, New York.

A CASE OF POROKERATOSIS MIBELLI LIMITED TO ONE SIDE OF THE BODY. OTTO KONRAD SCHOLL, *Dermat Wehnschr.* **72**:1 (Jan.) 1921.

The disease occurred in a child, 16 months old, and was limited to the left side of the body. Epileptiform attacks began about the same time as the skin affection. Treatment was given with carbon dioxid snow.

KETRON, Baltimore.

DERMATITIS EXFOLIATIVA OF THE NEW-BORN, WITH EXTENSIVE FISSURES OF THE LIPS AND CHIN. G. THIBIERGE and J. STIASSNIE, *Bull. Soc. franç. de dermat. et syph.* **1**:15, 1921.

A baby, 1 month old, presented the picture of Ritter's disease, which had appeared ten days after birth. The peribuccal fissures resembled those of syphilis, which condition was excluded only after careful investigation of the patient and his parents. The patient was breast-fed, and showed a satisfactory gain in spite of the dermatosis.

PARKHURST, New York.

LYMPHANGIOMA CIRCUMSCRIPTUM. HUDELO and PICARD, *Bull. Soc. franç. de dermat. et syph.* **3**:80, 1921.

A girl of 22 years presented, in the left thorax, a spongy tumor measuring 3 by 4 cm. at the skin level, but somewhat more extensive beneath. Clinically and microscopically it showed the typical picture of hemolymphangioma.

Balzer recalls a case of extensive lymphangioma involving the lower abdomen, inguinal and genitocrural regions.

PARKHURST, New York.

A CONTRIBUTION TO THE KNOWLEDGE OF MELANOTIC TUMORS. WALTER TREUHERZ, *Dermat. Wehnschr.* **71**:963 (Nov.) 1920.

The author reports a case of generalized melanotic carcinoma in a woman, 26 years of age, resulting from the cauterization of a nevus on the back. Death followed within eleven months. The patient became pregnant soon after metastasis of the tumor had begun and gave birth to a child weighing 1,440 gm. a short while before her death. The child died within a few days of undernutrition and at necropsy no evidence of malignant growth was found.

KETRON, Baltimore.

AN OLD UNDETECTED SYPHILITIC PERIOSTITIS. TRAUMATISM BY A BULLET: A CONSECUTIVE TERTIARY CUTANEOUS SYPHILID "IN SITU." CLEMENT SIMON, Bull. Soc. franç. de dermat. et syph. **3**:82, 1921.

In November, 1916, a soldier received a bullet wound in the left forearm; it healed rapidly. In April, 1917, small nodules appeared in the scarred region; they disappeared spontaneously, to return in February, 1918. In April, 1918, he was seen by the author, who found the cutaneous lesions to be typical of tertiary syphilis. A radiograph showed extensive bilateral ulnar osteoperiostitis, and it was noted that the syphilitic scar was bound to the ulna. It is thought that the bullet wound, involving syphilitic periosteum, set free spirochetes which caused the subsequent cutaneous manifestations. The traumatism may have been a predisposing factor.

PARKHURST, New York.

NERVE INJURIES DUE TO ERRORS IN TECHNIC IN MAKING INTRAVENOUS ARSPHENAMIN INJECTIONS. D. LEWIS, J. A. M. A. **76**:1726 (June 18) 1921.

Arsphenamin injected into or about a nerve may have a marked destructive action, causing extensive degeneration of neuraxes and consequent deformities and other manifestations in the area of distribution of the injured nerve. Two cases are reported in which technical error in arsphenamin administration resulted in severe median nerve injury. The possibility of such a mishap is another reason for the exercise of extreme care in arsphenamin injections.

MICHAEL, Houston, Texas.

A CASE OF SYPHILITIC REINFECTION. CLEMENT, Bull. Soc. franç. de dermat. et syph. **3**:106, 1921.

In 1918, a Serbian soldier, 33 years of age, presented symptoms of secondary syphilis, including lymphadenopathy, loss of hair and headache, together with a strongly positive Wassermann reaction; there was no history of chancre. Within five months a total of 15.25 gm. of neo-arsphenamin was administered, and his Wassermann reaction became negative.

In December, 1919, he was exposed to syphilitic infection and on Jan. 10, 1920, he presented a typical chancre of the balanopreputial fold, in which *Spirochaeta pallida* was found. This time mixed treatment was administered, and there were no further symptoms of syphilis.

PARKHURST, New York.

THE TOXICITY AND TRYPANOCIDAL ACTIVITY OF SODIUM ARSPHENAMIN. J. F. SCHAMBERG, J. A. KOLMER and W. D. RAIZISS, J. A. M. A. **76**:1823 (June 25) 1921.

The highest tolerated dose of sodium arsphenamin administered intravenously to white rats was found to be from 212 to 215 mg. per kilogram of weight. The average tolerated dose of arsphenamin was 105 mg. and of neo-arsphenamin 200 mg. per kilo.

Using rats infected with *Trypanosoma equiperdum* as test animals, these investigators found the therapeutic dose of sodium arsphenamin to be from eight to thirteen times less toxic than the highest tolerated dose. Arsphenamin

shows a ratio of dosis curativa: dosis tolerata of 21, and neo-arsphenamin a ratio of 22.

Thus, sodium arsphenamin possesses the low toxicity of neo-arsphenamin, but has a distinctly less curative value than either arsphenamin or neo-arsphenamin.

MICHAEL, Houston, Texas.

A CASE OF FETAL ICHTHYOSIS (BENIGN FORM). G. THIBIERGE and P. LEGRAIN, *Bull. Soc. franç. de dermat. et syph.* **1**:8, 1921.

This case will be considered in an article soon to appear in the *Ann. de dermat. et syph.* A girl, 14 years old, with a negative family history had, since birth, presented a hyperkeratosis with a predilection for the flexures. There was a palmar and plantar keratoderma with hyperhidrosis, and a seborrhea of the scalp. The nails were markedly involved. Noteworthy points were the comparatively slight facial involvement, the absence of malformation of the lips, eyelids and nares, and the accompanying erythroderma; there were no bullae. Brocq classifies this as erythrodermie congenitale ichthyosiforme with hypertrophy.

PARKHURST, New York.

TREATMENT OF PSORIASIS WITH INTRAVENOUS INJECTIONS OF 20 PER CENT. STERILE SOLUTION OF SODIUM SALICYLATE. OTTO SACHS, *Wien. klin. Wchnschr.* **34**:185, 1921.

Since 1918, Sachs has treated thirty-four patients with psoriasis with intravenous injections of sterile sodium salicylate in 20 per cent. solution as follows:

First dose (10 c.c. of solution) 2 gm, followed in two or three days by 3 gm.; after two or three more days 4 gm. This dose is not exceeded. The total dosage required is from 21 to 28 gm. The injections are well borne, and the patients seldom complain.

Recent cases are most easily benefited. Inveterate psoriasis is difficult to control, and recurrence has been noted. The method is especially applicable in widespread cases in which massive external treatment is contraindicated.

The author is also working with aqueous solution of aspirin in psoriasis.

GOODMAN, New York.

TWO CASES OF ORIENTAL BOIL. GASTOU and PONTOIZEAU. *Bull. Soc. franç. de dermat. et syph.* **1**:19, 1921.

Both patients had been at Biskra, and they thought mosquito bites were causative. The lesions were on the lower extremities; they were multiple. In the first case the lesions were of very short, in the second of longer, duration. Considerable painless lymph-node enlargement was noted in the second case. By way of efficient treatment, Darier recommends the intravenous administration of tartar emetic once or twice a week in increasing doses. This must be given slowly, to avoid respiratory embarrassment.

PARKHURST, New York.

TWO CASES OF PARAPSORIASIS GUTTATA. GASTOU and PONTOIZEAU, *Bull. Soc. franç. de dermat. et syph.* **1**:22, 1921.

Both patients presented small papulosquamous, nonpruritic lesions with a general distribution, resembling those of lichen planus. In one case the urine contained a slight amount of bile pigment.

PARKHURST, New York.

ARSPHENAMIN TREATMENT OF PULMONARY GANGRENE. BELA MOLNAR, JR., Wien. klin. Wchnschr. **34**:255, 1921.

Arsphenamin has been found efficacious in pulmonary gangrene. Results are directly proportionate to the time after infection that the arspenamin was injected. Early cases give the best prognosis.

GOODMAN, New York.

A CASE OF LEPROSY FROM ROUBAIX. CASTEL, Bull. Soc. franç. de dermat. et syph. **1**:23, 1921.

A Frenchman, 36 years of age, presented the nodular type of eruption in the usual locations. The incubation period was between six and seventeen years, the patient having been in the tropics during the supposed time of exposure. The Wassermann reaction was feebly positive. Hansen's bacilli were found in the nodules and sparsely in the nasal secretions.

PARKHURST, New York.

THE TREATMENT OF LUPUS BY FINSSEN THERAPY. L. BIZARD, Bull. soc. franç. de dermat et syph. **4**:138, 1921.

It has been justly claimed that this method of treatment is tedious and expensive, but, as the author shows, it is most effective. Before a cure is pronounced, six months must have elapsed without a sign of recurrence. In the 457 cases treated the results have been as follows: Lupus vulgaris in 414 cases, 106 cures; lupus erythematosus in 21 cases, 6 cures; suppurating tuberculous adenitis in 22 cases, 8 cures. The other common methods of treatment are often advantageously combined with the Finsen therapy.

PARKHURST, New York.

CONCERNING A COMBINATION TREATMENT METHOD OF SUGAR AND ARSPHENAMIN. VIKTOR PRANTER, Wien klin. Wchnschr. **34**:183, 1921.

Pranter has reported on the use of grape sugar solution followed by arspenamin in the treatment of syphilis. (Abstracted in these ARCHIVES **3**:657, 1921.) He has gradually reduced the interval (twenty hours) between the two injections until at the present time he is dissolving the neo-arsphenamin in the grape sugar solution. The solution is said to be more stable than the water solution.

Brief case reports are given, which mention favorable results using this combination, although the doses of neo-arsphenamin were small, 0.15 gm. Several patients with psoriasis also showed improvement with this medication.

GOODMAN, New York.

A CASE OF PROBABLE LICHEN PLANUS OF THE DORSUM OF THE TONGUE. G. THIBERGE and P. LEGRAIN, Bull. Soc. franç. de dermat. et syph. **4**:147, 1921.

The patient, 20 years of age, presented a noncharacteristic white plaque on the lingual surface, with a border of minute white punctae; along the interdental line of the right cheek there were two similar patches. The usual fine meshwork of lichen planus was lacking, but a biopsy examination showed the structure of lichen planus rather than of leukoplakia. There were no lesions of lichen planus elsewhere.

PARKHURST, New York.

A TECHNIC OF INTRAMUSCULAR (EPIFASCIAL) INJECTION. JOHN H. STOKES, Med. Rec. **99**:7 (April) 1921.

For these injections the author favors the inner and lower aspect of the upper outer quadrant of the buttock. The patient should lie prone on a table, be completely relaxed with the legs moderately rotated internally and arms hanging loosely over the edge of the table. Twenty-two gage needles are used, the length ranging from $1\frac{1}{2}$ to $2\frac{1}{2}$ inches, depending on the amount of subcutaneous fat. The buttock is drawn firmly downward with the left hand, and the needle introduced slightly inward and downward at an angle of 20 degrees. An attempt to aspirate is preferred to the removal of the syringe to determine whether the needle end rests in a blood vessel.

If the technic is carefully followed, the contents of the injection will be deposited in the areolar tissue on the upper surface of the fascia covering the gluteus maximus and result in less local irritation and more rapid absorption.

Various errors of technic are pointed out and their remedies given.

TOMLINSON, Omaha.

MYCOSIS FUNGOIDES IN A NATIVE OF MOROCCO. DECROP and SALLE (LACAPERE), Bull. soc. franç. de dermat. et syph. **4**:148, 1921.

Mycosis fungoides has rarely been observed in the natives of North Africa, hence this report. A Moroccan, 50 years of age, who had had the disease about ten years, presented a fairly generalized eruption with several small ulcerating tumors, one of which was excised. Histologic examination confirmed the diagnosis. The patient disappeared.

PARKHURST, New York.

SOME REMARKS ON THE DEVELOPMENT OF THE LEISHMAN-DONOVAN BODIES. J. E. R. McDONAGH, Proc. Roy. Soc. **14**: No. 6. April, 1921.

The author reviews three cases in which Leishman-Donovan bodies were found. In one case, following a wound, there developed discrete granulomatous papules at the edge of the scar and similar lesions on the penis. In a second case, a man aged 52, had never been free of scattered cutaneous lesions which appeared suddenly as small papules, to become furuncles, then ulcers, finally healing after a crust had fallen off, leaving deep scars. The third patient presented a single lesion on the cheek resembling a frambesiform syphilid. Tissue removed from all three cases revealed strikingly similar pathology. There were present three zones: an outer layer of plasma cells, then a layer of plasma cells, lymphocytes and endothelial cells, and a center composed of endothelial cells. Typical Leishman-Donovan bodies were recovered in each case. The author speaks of *Leukocytozoon syphilidis*, and noting clinical resemblance between syphilis and Leishmaniosis, suggests that the Leishman-Donovan body is the mature form of an asexually produced protozoon which would suitably be named *Leukocytozoon Leishmania*.

GUY, Pittsburgh.

EPITHELIOMA OF THE TONGUE IN A MOROCCAN. DECROP and SALLE (LACAPERE), Bull. soc. franç. de dermat. et syph. **4**:149, 1921.

Visceral cancer in general is conceded to be a rarity in North Africa, but this does not apply to cancer of the skin. The authors have seen twenty-four

cases. Epithelioma of the tongue, however, is sufficiently rare to warrant the report of this case. A Moroccan, 50 years of age, who had contracted syphilis sixteen years previously, presented a typical lingual epithelioma, proved by biopsy. He refused treatment.

PARKHURST, New York.

THE INFLUENCE OF RARE EARTH SALTS ON THE INOCULABILITY OF THE LESIONS OF CUTANEOUS TUBERCULOSIS.
C. LAURENT, *Bull. soc. franç. de dermat. et syph.* **4**:150, 1921.

Four patients, presenting scrofuloderma, lupus vulgaris and tuberculosis mucosae orificialis, were given two or three series of twenty intravenous daily injections, monkeys being inoculated after each series. All the inoculations were "takes," which proves that the bactericidal power of this medication is nil.

PARKHURST, New York.

THE OCCURRENCE OF PELLAGRA IN PATIENTS APPARENTLY RECEIVING AN AMPLE DIET. W. F. TANNER and G. L. ECHOLS, *J. A. M. A.* **76**:1337 (May 14) 1921.

An institutional patient, who was apparently receiving a liberal dietary, developed pellagra. Investigation showed, however, that the patient had been eating cereals and vegetables almost exclusively, though the meals included beef and milk.

The authors cite this instance to warn against the assumption that because a patient is provided with a certain diet this also is eaten. Unless this is remembered and the actual consumption of food investigated, occurrences of this sort would prejudice clinicians against the dietary etiology of pellagra. There is danger of drawing erroneous conclusions when the knowledge in hand concerns the available food supply rather than the diet actually consumed by the patient.

MICHAEL, Houston, Texas.

FOUR CASES OF HEREDITARY MONILETHRIX IN MOROCCANS.
E. LEPINAY, *Bull. soc. franç. de dermat. et syph.* **4**:152, 1921.

Two young brothers, the father and the grandmother presented scalps typical of this affection. A third brother, who had died, was said to have had the same trouble. The eyebrows and lashes were always intact. Incidentally, the brothers were found to be congenitally syphilitic, with strongly positive Wassermann reactions.

PARKHURST, New York.

SYNDROME OF FAMILIAL EXOPHTHALMIC GOITER. LEREDDE and DROUET, *Bull. soc. franç. de dermat. et syph.* **4**:142, 1921.

In these cases, according to the authors, there is always some etiologic factor; they are never "essential." Some are syphilitic in origin; this is one of the several syndromes which may be produced by syphilis. This must be kept in mind and syphilis must be sought for and treated before other therapeutic measures are tried. The authors report a case in which neo-arsphenamin was effective.

PARKHURST, New York.

RADIUM THERAPY. G. RIEHL, Wien. klin. Wchnschr. **34**:182, 1921.

Riehl reviews the subject of radium in therapy, and recommends the use of its rays following operative procedures on superficial malignancies to avoid recurrence in the scar and for the following skin diseases: lupus vulgaris, scrofuloderma, lupus erythematosus, nevus vasculosus, hypertrophic scars, keloids, chronic eczema, lichen Vidal and leukoplakia oris.

Since the cost of radiation to some patients is prohibitive, the property of radium emanation should be utilized. For the Vienna hospitals, radium emanation is prepared at the radium station, standardized, dosage noted as for day to be used and delivered, sometimes by post. Preparations are so made as to contain the desired dosage on day of receipt. Emanation loses more than 25 per cent. of its activity in less than four days, and after thirty-eight days possesses none at all.

The radium station also prepares emanation to be sold through pharmacies on physician's prescription.

GOODMAN, New York.

LYMPHANGIOMA OF THE BUTTOCK. PAUTRIER and O. ELIASCHEFF, Bull. Soc. franç. de dermat. et syph. **4**: R. S. 20, 1921.

A child of 9 years had had the malformation for eight years; its length, when first observed by the authors, was 12 cm. and it was 9 cm. wide. There were vegetations, resembling those of tuberculosis verrucosa cutis and many vesicles. The lower third of the derma was not involved. Treatment by cautery was proving most effective.

PARKHURST, New York.

A CASE OF URTICARIA PIGMENTOSA IN AN ADULT. O. ELIASCHEFF, Bull. Soc. franç. de dermat. et syph. **4**: R. S. 17, 1921.

A woman, aged 34 years, presented the typical manifestations of the disease, which she had evidently acquired during adult life. The usual intercollagenous mast cells were found in considerable numbers, although not forming a tumor. The etiology is still obscure.

PARKHURST, New York.

THE WHITE ADRENAL LINE (SERGENT); ITS CLINICAL SIGNIFICANCE. W. E. KAY and S. BROCK, Am. J. M. Sc. **161**:555 (April) 1921.

The adrenal line consists of a blanching of the skin following light stroking by a blunt object. It is pure white with no red element, lasts several minutes and is supposed to indicate hypo-adrenia, according to Sergeant.

Two hundred and fifty-five cases were studied, and the assertion is made that the so-called white adrenalin line of Sergeant is a local vasomotor reflex, resident in the skin and bears no direct relationship to adrenal gland activity. It was found to be independent of blood pressure, acute fatigue or other signs of hypo-adrenia; it occurred in normal persons and was peculiarly associated with scarlet fever. The vasomotor state allowing its best exhibition was found in young adults, especially those with scarlet fever.

JAMIESON, Detroit.

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, May 25, 1921

JAMES MCF. WINFIELD, M.D., *President*

EPIDERMOLYSIS BULLOSA. Presented by DR. WISE for DR. FORDYCE.

A. C., a 3-year old boy of American birth, presented bullae in various stages, averaging about 2 cm. in diameter, sparsely scattered over the trunk and extremities. The sites of recent bullae were denuded of epidermis, and the older sites were pigmented. The oral mucosa was not involved. In the ears and on the fingers especially were seen the characteristic epidermal cysts of millet seed size. The nails of all the fingers and toes were absent, having been lost at the age of 10 months. The patient's three older brothers and sisters were normal, the parents likewise.

The diagnosis was accepted without dissent.

CASE FOR DIAGNOSIS (EPIDERMOLYSIS BULLOSA?). Presented by DR. BECHET.

L. R., aged 6, from Dr. Trimble's service, had had the eruption for which he was presented since the age of 6 months. The father stated that while the child underwent acute exacerbations from time to time, he had never been entirely free during that period. He also stated that the eruption at the time of presentation was at its worst. It consisted of grouped, sharply margined, orbicular patches surrounding the eyes and the mouth. These patches seemed erythematous and vesiculobullous. The eruption was also present around the genitals, on the hands and legs, and in the mouth. There were small distinctly bullous lesions on the fingers and the remains of what might have been bullae on the tongue. There was an extensive alopecia, which the father said was always worse with the increase of the eruption elsewhere. With the involution of the eruption the hair returned. There were no lesions on the scalp. The patient's health seemed much below par. The Wassermann reaction was negative.

NEVUS LIPOMATODES. Presented by DR. SHERWELL.

Mrs. V. V., aged 22, a decided blond, presented a nevus lipomatodes on the forehead. A slight discoloration was present on the patient from birth. The parts affected were the right side of the nose, extending over the forehead to the border of the hairy scalp on that side.

DISCUSSION

DR. SHERWELL said that he had had a number of cases in which it was claimed that the condition was due to prenatal impressions, and he could not but feel that such claims were entitled to some credit. He knew, of course, the anatomic and physiologic objections, and of course it went without saying

that profound impressions made on the mother were not always followed by ill results; but that an intensely vivid impression might in some instance produce some such effect was not beyond credence and was supported to a certain extent by the widespread belief extending through the ages. In the lower animals he had observed many striking instances of this possible fact but could not in the press of time present them.

CASE FOR DIAGNOSIS. Presented by Dr. TRIMBLE.

G. M., a woman, aged 45, born in the United States, had suffered for two years with superficial erosion of the gums. Viewed clinically, the disease seemed to be an exfoliation of the epithelium; this exfoliation occurred at frequent intervals and during an attack the various size areas would be raw in appearance. The patient claimed that the lesions started as blebs which would later rupture and peel off, although no distinct vesicles or blebs had been noticed by the presenter. The eruption produced both pain and burning, and interfered with eating. She had consulted numbers of dentists and physicians without relief.

DISCUSSION

Dr. WISE inquired whether Dr. Trimble had ever read what Sutton stated about peri-adenitis mucosa necrotica recurrens, in his textbook.

Dr. TRIMBLE replied that he had discussed the subject (peri-adenitis) with Sutton personally, several years ago. The patient was free from the lesions at times for a week or ten days, and then they would recur. The woman's husband stated that she had had one or two attacks, diagnosed by the family physician as gallstone colic. Dr. Whitehouse then inquired whether any of the members thought the condition might represent a beginning pemphigus.

Dr. HOWARD FOX said that his case, to which Dr. Wise had referred, was not like the one presented. It was similar to the condition described in the textbook of Dr. Sutton as a recurrent peri-adenitis of the mucous membrane.

Dr. WILLIAMS thought it was a chronic infectious process and that the diagnosis could probably be determined by a careful microscopic and cultural examination of pus obtained from the gums.

Dr. POTTER agreed with Dr. Williams, and told of two similar cases at the Long Island College, one of which had been studied for a year, all examinations to determine the etiology being negative. It was finally decided that it was due to some infectious process, the cause of which could not be determined. It improved under treatment for such a condition, but never entirely cleared up.

Dr. TRIMBLE said that in this case a culture had shown some form of staphylococcus; vaccines had been made and used on the patient without any effect. He did not think it could be peri-adenitis mucosa, for he had understood that the condition which Sutton described was nodular, sloughing and deeper seated. The condition in the patient just shown was a superficial exfoliation of the mucous membrane, especially on the gums.

CASE FOR DIAGNOSIS (LESION OF THE GLANS PENIS). Presented by Dr. HOWARD FOX.

A. C., a dentist, aged 49, had suffered for the past seven or eight years from recurring attacks of small vesicles on the under surface of the glans penis. They had lasted for a few days, as a rule, and had given rise to no sub-

jective symptoms. The lesions never ruptured nor formed crusts. The condition as presented was first noticed five months ago and had remained practically unchanged since then. It consisted of an elevated circumscribed patch on the left side of the under surface of the glans, composed apparently of closely crowded shiny vesicular lesions. On puncture with a needle, a tiny drop of clear fluid escaped. A portion of the patch had lately been cauterized by a physician with silver nitrate. There was no palpable enlargement of the inguinal glands.

DISCUSSION

DR. WHITEHOUSE said he could throw little light on the case, but he could not feel that such an eruption continuing for that length of time, even though the vesicles were there, was a simple thing like herpes. It might be a rare type of Paget's disease. It was certainly worth considering along that line.

DR. HIGHMAN said it was very difficult to formulate a clinical opinion, but he thought it was epithelioma. On account of the obvious importance of making a correct diagnosis, the matter should be decided by a microscopic examination. A biopsy should be performed and the diagnosis made while the patient was on the table. If unfavorable, either the actual cautery or treatment as recommended by Pfahler of Philadelphia should be used, followed by roentgen ray or radium therapy, subject, of course, to the opinion of the surgeon. If any procedure was carried out locally, it ought to be followed by roentgen-ray therapy on both groins. The whole treatment, however, rested on accurate microscopic study of the case.

DR. TRIMBLE said that the lesion impressed him as an epithelioma of the superficial basal cell type, pretty much the same thing as Paget's disease. It was hard, however, to reconcile that diagnosis with the vesicles on the border of the lesion. He had seen a case very much like this, but with no vesicles on the border. He would certainly remove a small piece for microscopic examination.

DR. G. H. FOX said that the lesion had persisted for some five months, and that if it continued for five months longer it would probably look more like epithelioma than it did now.

DR. KLOTZ said he did not feel sure that the lesion was an epithelioma. Perhaps the removal of the prepuce would do away with the irritation by the constant friction and establish more favorable conditions for healing.

DR. KINGSBURY expressed the opinion that at the present time the case called for conservative therapy. From the history the man had evidently been badly treated; he had had stimulation and various applications and it might be better if he had not been treated at all. It was the type of case that might very easily develop into epithelioma.

DR. WISE said that the occurrence of vesicles made him think of lymphangiectodes. The diagnosis of epithelioma was a risky one to make, whereas there were undoubted fluid lesions suggesting lymphangiectodes. These occurred frequently on the scrotum but were rare on the penis. That was the only diagnosis he could think of, taking into consideration the vesicle formation.

DR. HIGHMAN said that from the diversity of opinion that had been expressed he could not see any harm in a conservative procedure such as he had suggested.

DR. HOWARD FOX asked what Dr. Wise would suggest as a diagnostic procedure.

DR. WISE replied that he would not make a biopsy on the glans penis, but would treat the case as Dr. Highman had suggested. The best interest of the patient called for the destruction of the growth rather than determining what it was, unless one was sure it was an epithelioma.

DR. TRIMBLE cited a case in which biopsy was made and the case proved to be epithelioma. He then did a curettage and cauterization, and five years later showed the patient before the Society, perfectly well.

EPIDERMOPHYTOSIS (THREE CASES). Presented by DR. WILLIAMS.

The first patient, Mrs. B. C., aged 35, complained of an intertrigo of the toes of both feet, with much swelling, burning and itching, which had been present since November, 1920. The pain and swelling was so great as to make walking difficult. She showed the maceration between the toes, with scaling at the posterior border of the inflamed area, typical of tinea infection. Mycelia were demonstrated in the scales, but the type of organism was not yet determined.

The second patient, Mrs. A. Y., aged 23, came to the hospital May 16. She had a localized eruption of deep vesicles on the sole of the right foot just behind the ball of the great toe, occupying an oval area about $1\frac{1}{2}$ by 2 inches. The eruption was not intense in the center of this area, and the border was indefinite. She had a similar smaller group of deep vesicles on the radial surface of the left little finger. Mycotic organisms were demonstrated from both the hand and the foot. She was given Whitfield's ointment, half strength, and four days later returned with an acute vesicular outbreak on both hands and feet, involving palms and soles, the lateral surface of the fingers, and the dorsum of the right foot. Mycelia were demonstrated from a vesicle on the part of the foot first affected, but could not be found in the fresh vesicle on the dorsum of the foot. On both legs, both forearms, and on the upper part of the chest in front was a sparse erythematous eruption, consisting of pale pink oval, slightly elevated spots, about a quarter to a half inch in diameter, some of which presented a small vesicle which was sometimes in the center, sometimes at the periphery. The use of Whitfield's ointment was discontinued, and she was told to wash thoroughly with soap and warm water and to use calamin lotion. This she did, and within three days the eruption on the hands and feet was receding. The erythematous eruption on the forearms and legs persisted, and as presented bore a striking resemblance to pityriasis rosea, with pale center, and pink, slightly scaly, border, but without vesicles. Except for a few spots in the sternal region the trunk was free. Scrapings from the site of the original lesion on the foot, from a vesicle on the wrist, and from one of the lesions resembling pityriasis rosea were all negative.

The third patient, H. B., a boy, aged 9 years, came under treatment May 18, with a history of having had tinea for about eight weeks and kerion for three weeks, most acute during the early part of May. There had been much swelling of the scalp, especially of the right side, accompanied with exudation of sero pus. For the last three weeks the child had been restless and feverish at night, and had a poor appetite. The kerion was about 2 inches in diameter, with a few outlying spots. Spores were demonstrated in the hair. There was no eruption on the body. On May 18, the kerion was subsiding. Surrounding the neck, most marked on the sides, was an eruption of small, soft follicular papules. Those at the border of the area were flesh colored, the others becoming a deeper red and more elevated toward the center of the area involved.

There were some urticarial lesions on the forearm. On May 20, urticarial lesions were still visible on the forearm, but the papules on the neck were fading.

The first case was one of typical ringworm of the feet; the second, a case of ringworm of the sole of the foot and of the fingers, followed by an eruption which seemed to be a trichophytid. This was the second case Dr. Williams had seen of acute infection of ringworm of the hands, producing at the height of the process an eruption which seemed to be a trichophytid, and which subsided without antiparasitic treatment. The third case was kerion followed by papular trichophytid.

DISCUSSION

DR. HIGHMAN said it was a most interesting group of cases, representing what in the old days would have received internal treatment. He said that usually such cases made a circuit of all the dermatologists in the vicinity. The literature on the subject dated back some seven or eight years. Whitfield was the first English speaking author to write about it, while Ormsby and Mitchell deserved the credit of having popularized the subject in this country. On account of the war we almost lost sight of the fact that a number of men in Europe had investigated the matter. Since then every one seemed to think that the underlying condition was a fungus. Almost any pus producing fungus would cause such a picture. The case of the boy was the most interesting of the three. He suggested that Dr. Williams try cataphoresis.

DR. HOWARD FOX said that Dr. Williams' demonstration was very instructive and tended to call attention to the fact that many cases of so-called eczema were in reality due to some form of tinea. He regretted that he could not have shown a patient he had recently seen who presented nondescript dry, scaly patches on the extremities, together with a circinate, sharply bordered eruption on the inner aspect of the thighs and a typical onychomycosis (affecting one finger). The fungus was readily found in scrapings from the skin of the arm. The generalized eruption presented by a boy with kerion was a type that had not previously been presented before the Society. It was undoubtedly one of the so-called "trichophytids," representing a toxic or allergic reaction. He had recently seen two cases of more or less generalized eruption appearing in children with ordinary ringworm of the scalp, about two and a half weeks after roentgen-ray treatment. In these cases, there had not been the usual constitutional manifestations noted in cases with kerion ringworm. He called attention to the differences in type in these allergic cases as reported by Rasch and others. They were at times lichenoid or scarlatiniform, or like a seborrheic eczema in appearance.

DR. TRIMBLE said that he has been interested in this subject for some time, but would undoubtedly call the condition shown by the young woman in the center a pompholyx. He did not question what Dr. Williams found in both lesions, but would make the diagnosis of pompholyx regardless of what was found. He did not think that every case of pompholyx was caused by the epidermophyton, and he believed that if this young woman was treated as usual for that condition she would recover. The point he wished to bring out was that just because one found a fungus in association with a skin disease it should not immediately be concluded that it was the cause of the condition.

DR. BECHET asked if he was correct in understanding that in trichophytid one could demonstrate the fungus in the pustular lesions. In the so-called lichenoid trichophytids as described by Jadassohn, the lesions were frequently

associated with kerion. Rasch found that seventy-one of 109 cases were accompanied by kerion formation. The lesions were vesicular and pustular, and the trichophyton faviforme discoides was cultivated from the contents of these lesions.

DR. WILLIAMS said that the woman had a typical case of ringworm of the toes. The other two cases he believed were both trichophytid. The boy had a distinct kerion and suffered from the restlessness, sleeplessness and feverishness usually found in cases giving a distinct history of trichophytid. When first seen the eruption was marked, but had faded since that time. He had seen two other cases at the Skin and Cancer Hospital within the last two months. In another case of kerion seen in the Post-Graduate Hospital, in the service of Dr. Whitehouse, there was a distinct lesion resembling lichen scrofulosorum on the neck. The boy also showed two lesions on the neck resembling tinea circinata, but no organisms were found. As Dr. Fox had pointed out, a number of these cases had been described by various authors. The lesions that had been described were papular, like erythema multiforme, and like scarlatina, pustular and vesicular.

A patient seen last March at the Skin and Cancer Hospital had a temperature of 103, with a profuse eruption over the chest and arms, and papules forming lesions an inch or more in diameter. These cases regularly recover without treatment. The girl certainly went on to recovery without any treatment. The worse the kerion, the more quickly they got well and the more quickly the rash subsided.

Dr. Williams said further that he had always treated these cases with antiseptic ointment, but he thought that they would do just as well with the use of boric acid fomentations, which was considered the best treatment.

The young woman was the most interesting case. She undoubtedly had pompholyx, but that was simply a name for an eruption and told nothing of the etiology. The patients would usually get well in time, regardless of treatment. Whether or not Dr. Highman was right in saying that there were a number of different forms of pompholyx, some caused by toxins, he could not say. There was an increasing tendency to believe that most of them were caused by ringworm. Schrameck mentioned it particularly in the sole. That was the most definite lesion of tinea of the foot. The lesions on the sides of the fingers were the most difficult in which to find the organisms. On the sole they were fairly easy to find. It did not seem to be a case of epidermophytosis. The toes were not involved; and it seemed to be an infection with some form of trichophyton.

The great interest in the case was not in the finding of mycelia, but in the fact that there was a sudden outbreak over both soles and over the palms and legs. It seemed to be a case of trichophytid caused not by the spread of the organism but by the spread of the toxins, and was to be accounted for by the distribution of the toxins through the system. The patient had had a localized eruption for weeks, and then at the end there was a sudden outbreak of distinct vesicles, followed by quick recovery. She produced her own antitoxins and recovered. She showed no improvement under Whitfield's ointment, but did show improvement under the use of soap and water. It was difficult to say, however, whether or not that had anything to do with the cure. She seemed to have reached the climax of the disease, and acquired immunity.

He then cited an almost identical case with lesions on the hand, appearing on the little finger and spreading over the hand. After a month, following the use of vaselin, a severe outbreak occurred over both hands and up the arm as far as the elbow. The patient did not improve under Whitfield's ointment, but under the use of soap and water got well quickly. There were cases reported of trichophytid following cases of tinea of the scalp or beard, but he did not know of any following tinea of the extremities. He was not aware of any cases of trichophytid that had been reported before the Society or anywhere in America.

URTICARIA PIGMENTOSA. Presented by DR. HOWARD FOX.

This patient had previously been reported at the last meeting of the Dermatological Section of the Academy of Medicine, on May 2. Since then the histologic examination by Dr. Highman had been completed. He reported a failure to find mast cells in the section. The Wassermann reaction had also been performed since the last meeting and was negative.

DISCUSSION

DR. HIGHMAN said that clinically the case was urticaria pigmentosa, but he had not been able to find mast cells. Hartzell had taken up the question before the American Dermatological Association and claimed that one could not make a diagnosis histologically without finding the mast cells in some of the lesions presented by the patient. Dr. Highman said that he himself had no doubt that the condition occurred in adults. Clinically, the case was urticaria pigmentosa, and he did not see why it could not be acquired.

SCLERODERMA. Presented by DR. WHITEHOUSE.

The patient was a woman showing a generalized scleroderma with sclerodactylia, and an unusual feature not before noted—atrophy of the tongue. The woman was about 46 years old, a native of Poland. She stated that the trouble began three months after her marriage, twenty-three years ago. She had had five children.

Dr. Whitehouse said that the condition seemed to be opposed to acromegaly, and asked the opinion of the members as to whether treatment with pituitary extract might produce any benefit.

The diagnosis was accepted without dissent.

HYDROA VACCINIFORME. Presented by DR. WHITEHOUSE.

The patient was a boy 8 years of age, and the condition had developed four years previously, when he had had scarlet fever. When first seen in November, he had no vesicles and showed only a few smallpox-like scars, but on appearing again recently he showed classical vesicular lesions of hydroa vacciniforme. He had had three attacks of the eruption since November. The storms of winter and the heat of summer alike seemed to provoke the attacks. The eruption was confined to the exposed portions of the body—the hands, face and ears.

This patient recalled another patient whose case he had presented three years ago—a little girl who was playing on the edge of a brook in the winter time, and the strong light of the reflected sun provoked the outbreak.

The diagnosis was accepted without dissent.

CASE FOR DIAGNOSIS. Presented by DR. WHITEHOUSE.

M. M., a man, aged 32, stated that the eruption exhibited had been present for six weeks. It began on the anterior surface of the right forearm, and soon thereafter appeared on the right side of the neck, front of the thighs, and back of the knees. The scalp and face were entirely free. The lesions were erythematous and presented little or no scaling. On the right arm they formed an aggregated patch involving most of its anterior aspect. At the lower part of this patch were distinct follicular lesions. On the right side of the neck they were plainly lichenified. There was also some lichenification on the thighs, and the lesions in that location were somewhat papular in appearance. The eruption was dry, and the patient stated that it was very pruritic. This was belied, however, by the absence of scratch marks.

DISCUSSION

DR. BECHET said that he had observed the case that afternoon by daylight, and in his opinion it resembled a seborrheic eczema.

DR. G. H. FOX said he would make the diagnosis of a follicular type of papular eczema. One of the best photographs he had ever taken was of a man whose thigh and leg were covered with follicular papules without any coalescing of the lesions. There was scarcely a follicle that was not inflamed.

LUPUS ERYTHEMATOSUS. Presented by DR. WILLIAMS.

Mrs. R. M., aged 26, born in the United States, gave an irrelevant past history. The eruption presented began four years ago as a small red pimple. The lesion left a small red patch which had spread since. It had been of the size exhibited for almost two years. There was slight scaling until a year ago. It had been treated by ointments for eczema. Since February she had under a doctor's direction, applied camomile tea, which gave rise to the present heaped up appearance of thick black adherent scales. She stated that the lesions itched at times. She presented a single lesion on the right cheek about the size of a twenty-five cent piece. The border was ill-defined, with a thin adherent grayish-green crust. Over the bridge of the nose and on the contiguous borders of the cheeks on both sides was a sharply defined lesion covered with a thick, hard, heaped-up black adherent crust. On removal of a fragment of this at the border, "pegs" were demonstrated.

LUPUS ERYTHEMATOSUS. Presented by DR. WINFIELD.

A. F., male, aged 29, born in Russia. One year ago a papule about the size of a ten cent piece appeared on the chin. This rapidly became covered with a thick black crust. Soon similar lesions appeared on the lip, bridge of the nose, side of the cheek, and back of the ear. The one on the cheek had involuted, leaving a white scar; the lesion on the lip was the size of a large split pea, was ulcerated, and had a slightly indurated border. The other lesions were covered with a thick black crust.

When first seen, the diagnosis of syphilis was entertained; but as the Wassermann and therapeutic tests were negative the diagnosis of lupus erythematosus was made. The case was shown because of the intensely black color and thickness of the crust.

DISCUSSION

DRS. BECHET and SCHWARTZ both thought the lesion in Dr. Williams' case lupus erythematosus, and this diagnosis was generally accepted.

ONYCHOMYCOSIS. Presented by DR. HOWARD FOX.

I. S., aged 23, born in the United States, a traveling salesman, first noticed the disease of the nails about two years ago, while he was still in military service. The nails of the left hand became affected one after another during a period of six months. Previous to the nail disease he had suffered from a scaly eruption of the left hand for ten months. Examination showed marked dystrophic changes of all the nails of the left hand, the other finger nails and toe nails being normal. There was no evidence of paronychia. Microscopic examination of scrapings from one of the affected nails was positive.

SYPHILIS (?). Presented by DR. WISE for DR. FORDYCE.

Mrs. M. M., an Irish housewife, aged 58, had possibly been infected with syphilis at marriage, sixteen years previously, but had never been treated for it. For the past year, there had been unusually exuberant nodular serpiginous lesions on the posterior surface of the left leg, including the popliteal space. At the time of presentation there was some ulceration, as well as central pigmentation and atrophy. The lower third of the leg showed a varicose dermatitis. (Subsequently there was a strongly positive Wassermann reaction, and a biopsy examination showed the lesions to be undoubtedly gummatous.)

DISCUSSION

DR. WHITEHOUSE said that from the multiplicity of the lesions, their distribution, and the character of the scars, he would consider the case syphilitic.

DR. POTTER agreed with Dr. Whitehouse.

DR. HIGHMAN said that clinically the case appeared to be syphilis. The lesions showed a lot of unusual granulation tissue, an atypical background with more or less of the characteristics of syphilis. If yaws could be ruled out, it was quite significant of syphilis. There was nothing to suggest sarcoid.

LEPROSY. Presented by DR. POTTER.

I. F., was a young man from Egypt who had lived in the United States for eight years. He stated that he had always been well excepting for an attack of malaria when a boy. About three years ago he first noticed a partial anesthesia of the little finger of the right hand, the condition finally involving all the fingers of that hand. At about that time nodules appeared on his entire body including the face and extremities. Many of these nodules broke down leaving open sores. There were no other subjective symptoms except occasional attacks of pain in the feet if not bandaged. As presented there were a number of raised purplish nodules on the face, hard and not painful to the touch. There was also a nodule on the cornea of the left eye and there were a few scars of former lesions. On the lower half of the legs and also on the lower part of both forearms were ulcerations in various stages.

The patient had received injections of chaulmoogra oil weekly for one year, and in addition one injection of arsphenamin, 0.3 gm., and three injections of silver arsphenamin, from 0.1 to 0.15 gm. Since treatment, the eye condition had improved.

DR. G. H. FOX reported further on the case of acanthosis nigricans presented at a previous meeting. He had seen the patient again and the inflammatory conditions having disappeared the case again presented only the symptoms described in the books as acanthosis nigricans. He hoped he would again have opportunity under more favorable circumstances of presenting this patient before the Society.

FRED WISE, Secretary.

PITTSBURGH DERMATOLOGICAL SOCIETY

*Regular Meeting, June 30, 1921*J. G. BURKE, M.D., *Presiding*

SARCOMA. Presented by DR. BOGGS.

A man, aged 48, who had had a small epithelioma removed from the lower lip nine years ago, was struck seven months ago on the chin, and a large tumor developed rapidly. A diagnosis of sarcoma was made, and it was concluded that the sarcoma was independent from the epithelioma. The growth was approximately the size of a small orange, was quite hard and fixed on the underlying bone.

DISCUSSION

DR. HOLLANDER agreed with the diagnosis.

DR. BOGGS stated that the patient was receiving radium treatment.

DYSHIDROSIS INFECTED WITH STAPHYLOCOCCI. Presented by DR. CRAWFORD.

A man, aged 32, a miner, noticed an eruption commencing on the palms and soles after working three months mining coal; most of this time his hands and feet were wet in sulphur water. The palmar surfaces became inflamed and covered with minute vesicopustules. The middle inner surfaces of the soles became likewise involved. The duration was six weeks. The periphery of the inflamed area of the soles suggested a trichophytosis, but microscopic examinations failed to reveal any fungus.

DISCUSSION

DR. GUY said that he favored a diagnosis of epidermophytosis and suggested that further search for the fungus be made.

DR. JACOB suggested multiple cultures from the edges of the lesions.

DR. SCHWARTZ thought that the condition should be classed as an occupational dermatitis due to constant maceration in sulphur water.

DR. CRAWFORD said that he had considered trichophytosis but had been unable to find the fungus. He felt that the clinical appearance and course of the condition justified a diagnosis of dyshidrosis.

MULTIPLE LIPOMAS. Presented by DR. BURKE.

A man, aged 37, for twenty years had noticed lumps appearing on his arms and legs and a few on his body. At the time of presentation the lumps numbered seventy and were mostly pea to hazelnut sized, except two which were as large as a walnut. The growths were subcutaneous, freely movable and seemed to follow the lymphatic glands. Several of the growths had been excised and a section of one was diagnosed as lipoma.

DISCUSSION

DR. CRAWFORD said that the location of the tumors along the course of the veins and in the loose areolar tissue favored the diagnosis as given. He felt that these growths should be classified as nevi.

DR. BURKE stated that the patient was very anxious to have something done and that he intended to insert radium needles in several of the growths to learn whether the radium would dissolve or liquify the fat.

SCLERODERMA. Presented by DRs. GUY, HOLLANDER and JACOB.

A woman, aged 34, nine months before had noticed swelling of the left leg, mostly below the knee and ten days later blackish spots near the knee, which became covered with scales and finally appeared as white atrophic scars. Similar lesions then appeared on the foot. Following this there developed a confluent linear lesion extending from the level of the great trochanter to the tip of the first and second toes. At the time of presentation there were two dime sized ulcers near the ankle. Near the thigh were numerous erythematous infiltrated plaques interspersed with depressed atrophic areas of the same size. The entire area was hard and sclerotic. The patient complained of much pain, especially at night. She had been on thyroid medication for some time prior to presentation and presented definite signs of hyperthyroidism. She also presented signs of arteriosclerosis and chronic nephritis.

DISCUSSION

DR. SNITZER called attention to the exophthalmos and suggested the possibility of endocrinous disturbance in a causal rôle.

DR. CRAWFORD agreed with the diagnosis and suggested the possibility of nerve injury on account of the distribution of the lesion and because the patient connected the appearance of the eruption with an injury to the hip. He felt that the ulcerations were trophic. He asked whether the urine had been searched for arsenic.

DR. HOLLANDER stated that the distribution of the lesion was compared with the dermadones of Djerden and no typical nerve distribution could be shown. He called attention to the fact that the knee jerk on the opposite side was increased, the consulting neurologist suggesting the possibility of a tumor of the cord located under the fourth or fifth lumbar vertebrae. He thought that the distribution of the eruption might be accounted for as following the line of venous return flow. He felt that the oversecretion of the thyroid was incidental to thyroid medication which was definitely contraindicated in this case.

LICHEN PLANUS HYPERTROPHICUS WITH BULLOUS LESIONS.

Presented by DRs. GUY, HOLLANDER and JACOB.

A man, aged 49, had a generalized eruption of six weeks' standing which differed in different parts of the body. On the forearm the lesions appeared symmetrically distributed, slightly more pronounced on the flexor surfaces. Individual lesions were typical of lichen, but the bulk of the eruption was confluent with slight scaling and somewhat verrucous in character. On both sides of the buccal mucous membrane a conglomerate patch of whitish quadrangular papules could be seen and felt. The lesions on the legs were more pronounced and shiny with the formation of circumscribed elevated verrucous patches. The right leg showed edema, and two bullous lesions were noted—one on a patch of lichen, the other bordering a similar patch.

PAPULONECROTIC TUBERCULID. Presented by DRs. GUY, HOLLANDER and JACOB.

A woman, aged 19 years, first noticed a papular eruption on her arms and legs fourteen months before presentation. The eruption would improve at times,

but new crops appeared at intervals. Since being under observation two crops had appeared. The early lesion was a firm papule which was soon capped by a small pustule. The center of the older lesions was depressed and black. The lesions left scars. Numerous large ecthymaform lesions were present on different parts of the body. She gave a history of gradual loss of weight, severe headaches, dizziness and nausea. The condition began about the middle of pregnancy and had gradually become aggravated. She gave marked symptoms of hyperthyroidism, including a positive von Graefe, Möbius and Rosenbach sign, and oculomotor test, and her basal metabolism showed a 31 per cent. increase. Local applications of various kinds were made with considerable improvement, but new crops would appear. About one month prior to presentation local treatment was discontinued and treatment by roentgen rays directed to the thyroid gland instituted. Since that time no new lesions had appeared, and the eruption and symptoms of hyperthyroidism were rapidly disappearing.

DISCUSSION

DR. CRAWFORD offered a diagnosis of ecthyma on account of the rapid onset, the pustular type of the lesions and a leukocytosis reported by the presenters.

DR. GUY was of the opinion that the similarity to ecthyma might well be attributed to secondary infection of typical lesions of papulonecrotic tuberculid.

DR. JACOB stated that regardless of the exact nature of the primary eruption, the leukocytosis could be accounted for by the considerable quantity of pus under the skin.

DR. HOLLANDER felt that there was a direct relationship between the hyperthyroidism and the eruption as evidenced by the disappearance of the eruption, together with improvement of the thyroid manifestations.

PSORIASIS CLEARED BY INTRAVENOUS USE OF FOREIGN PROTEIN. Presented by Drs. GUY, HOLLANDER and JACOB.

A man, aged 27, had appeared at the university dispensary with a typical generalized eruption of guttate psoriasis. Foreign protein in the form of paratyphoid vaccine was administered intravenously, beginning with one minum and ending with 36 minums. No local applications were made, and the eruption disappeared in fourteen days leaving only brownish spots in the sites of the lesions.

DISCUSSION

DR. CRAWFORD felt that a diagnosis of lichen planus should be considered on account of the pigmentation left by the lesions, the rapidity of evolution of the eruption and the presence of one suggestive papule on the forearm of the patient.

DR. GUY stated that the case was one of typical guttate psoriasis with a generalized eruption having a predilection for the bony prominences. The individual lesions were covered by abundant imbricated scales on removal of which fine bleeding points could be demonstrated. Subjective symptoms were entirely lacking. He stated that the case was presented only to demonstrate the effect of protein therapy in clearing the lesions; that he did not favor its employment except under unusual conditions, rather favoring the application of fractional doses of roentgen rays.

DR. BOGGS favored roentgen rays for clearing generalized psoriasis.

DR. JACOBS said that the method had been tried in the service of Drs. Engman and Mook and such pigmentations as those noted here were the rule; and that the method was only an alternate method of removing lesions, which would recur quite as promptly as after any other form of treatment.

DR. HOLLANDER said that any diagnosis other than psoriasis was untenable.

GLOSSITIS. Presented by DR. SNITZER.

A man, aged 46, born in Russia, a teacher, presented small shallow ulcerations on the edges of the tongue, which were of three years' duration. There were also several healed areas on the dorsal surface which were smooth and atrophic. There was no history of infection, no glandular enlargement and no edema of the tongue. In the preceding two years the lesions had cleared up at the end of the winter, and the patient had had no subjective symptoms. This year the lesions persisted, and he had a burning sensation at night.

DISCUSSION

DR. SCHWARTZ favored a diagnosis of syphilis. He felt that a Wassermann test and a vigorous therapeutic test would settle the question.

DR. SNITZER said that the patient had been put on specific treatment, although he doubted that the case was syphilitic. The lesions were also painted with silver nitrate which seemed to bring about marked improvement. Because of the specific treatment no Wassermann test had as yet been made.

CORRECTION

On page 256 of the August issue, the last word in the twelfth line from the bottom should be "reappear" instead of "disappear."

Book Review

LA DERMATOLOGIA NEI SUOI RAPPORTI CON LA MEDICINA INTERNA (DERMATOLOGY IN ITS RELATIONS TO INTERNAL MEDICINE). P. L. BOSELLINI, Professor of Dermatology of the University of Messina. One volume, 600 pages. Milano: Società Editrice Libreria, 1921.

Professor Bosellini has written a unique book. We do not know of any other treatise in the dermatologic literature covering so thoroughly and so scientifically the subject of the relation of internal disorders to dermatology. The first two chapters are dedicated to the anatomy and physiology of the skin, and these subjects are treated in detail. A special point is made of the description of the nervous system, particularly of the sympathetic. The third and fourth chapters deal with the pathologic anatomy and etiology of skin diseases, respectively. The second part of the book is the most important. It is dedicated to the study of the pathologic relations between the different organs and apparatus of the body and the skin. Professor Bosellini discusses the metabolism of fats in its relations to such diseases as xanthoma and seborrhea, the metabolism of carbohydrates and that of proteins and inorganic materials. Xanthoma is due to an excess of cholesterol in the body and the accumulation of this fatty substance in the tissues. Seborrhea is due to a disturbed metabolic activity of the epidermis and its appendages primarily and mainly caused by incomplete digestion of certain fats (butter) and of carbohydrates (potatoes and sugars). Especially interesting are the chapters on metabolism of carbohydrates in relation to diabetes and diabetic dermatoses and that of the proteins in relation to psoriasis, urticaria and eczema.

Bosellini calls "sympaticopathias" a series of dermatoses the etiology of which he finds in disturbances of the sympathetic nervous system, especially in its relation to the endocrine glands and to the trophic nutrition of the skin. These sympaticopathias are: cutaneous atrophy, scleroderma, Dercum's disease, gangrene, Raynaud's disease, keloid, edema angioneuroticum, zoster, alopecia areata, ichthyosis, dystrophies of the hair and other conditions.

There is a close relationship between the sympathetic system and the ductless glands and some authors believe that they form only one system which they call neuro-endocrine. The chapter on the relation of the internal secretions to dermatoses is limited, and it seems that the author should have given more extension and more importance to this subject. The chapters on digestive and respiratory systems in their relation to cutaneous disorders are interesting. Blood disturbances, especially the leukemias and their cutaneous symptoms, are well presented.

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Archives of Dermatology and Syphilology

VOLUME 4

OCTOBER, 1921

NUMBER 4

PSEUDOXANTHOMA ELASTICUM *

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BROOKLYN

AND

HERMAN GOODMAN, B.S., M.D.

WITH HISTOLOGIC REPORT BY D. S. D. JESSUP, M.A., M.D.

NEW YORK

HISTORICAL SKETCH

In 1884, F. Balzer¹ made a clinical and histologic study of a case which presented unusual and unique characters not theretofore described. The most conspicuous feature of the disease was its clinical resemblance to xanthoma, or xanthelasma, and its histologic changes which did not suggest the pathology of that condition. Fortunately, a complete and careful study of the patient was made both before and after death, so that there can be no question as to the identity of the disease.

In 1889, Chauffard reported a case as xanthelasma disseminatum et symmetricum. The patient was later examined and observations were published by Besnier and Doyen. Hallopeau and Lafitte also had the opportunity of studying the same patient.

In 1896, it fell to Darier's² lot to study the same patient. For the first time, histologic examinations were made, and the similarity to Balzer's case was recognized. Darier coined the name of pseudo-xanthoma elasticum, because the disease, although rare, had some clinical and histologic features which were so well defined that the disease deserved a name to distinguish it as a clinical entity. Histologically, the characters of fragmentation, with swelling, and finally complete degeneration of the elastic network merited the name "elastorrhesis," which appellation Darier has also given the disease.

* From the New York Skin and Cancer Hospital.

1. Balzer: Recherches sur les caracteres anatomique du xanthelasma, Arch. de physiol. norm. et path. Ser. 3, 4:64, 1884.

2. Darier: Pseudoxanthoma elastique, 3rd International Congress of Dermatology, London, 1896, p. 289.

Up to the present time, fifteen cases have been reported and six others mentioned in the literature.

Elastoma and nevus elasticus must be added to the names already given as having been applied, but pseudoxanthoma elasticum is most generally used.

COMPOSITE CLINICAL PICTURE

Pseudoxanthoma elasticum has presented great similarity of clinical features wherever it has been studied. It appears in youthful persons and in adults of both sexes, and more than one member of the family may be affected. The skin changes are usually symmetrical. The localizations of preference are the covered parts of the body, especially the regions of the great articular folds—the axillae, groins and bends of the elbows—and the uncovered portions, such as the neck, less often the hands and rarely the face.

The eruption consists of round or oval, hemispherical, smooth, shiny, pinhead (hempseed, millet seed, lentil seed) to pea sized papules. Their color may be mild yellowish mixed with violet, or less often brownish, ivory or colorless. The papules may be isolated, grouped, or confluent into plaques or linear formation. The clinical picture often gives the impression of a fine network, or meshlike pattern or trellis work. The affected areas may be surrounded by perifollicular spots of the same appearance formed of slightly prominent soft yellowish papules. The skin may be soft or slightly infiltrated, it may be wrinkled, and that of the articular folds may be greatly relaxed or even pendulous.

The affection remains limited for years or may increase in area. Change or evolution in the lesions or stage formation has not been previously mentioned. The subjective symptoms are nearly always absent, although mild itching has been noted.

Although several writers have referred to the lesions as xanthoma-like or xanthelasmatic, the clinical analogy to xanthoma is slight. The regions ordinarily the site of xanthoma are usually free in pseudoxanthoma elasticum, although localization on the face has been given. In one case it is admitted that the identity of the lesions on the face and those of pseudoxanthoma elasticum on the same patient could not be established.

COMPOSITE HISTOLOGIC PICTURE

The microscopic appearance, as given by various authors, may be described as follows: There is a change in the elastic fibers of the middle and deep portions of the corium generally considered a degeneration, and variously mentioned as a swelling, proliferation, splitting up and breaking up into fragments. Darier has termed this "elastorrhesis." Islands of these altered fibers, of different sizes, are found scattered

through the corium and surrounded by normal collagen. The transition between normal and degenerated elastic fibers has been noted. The changes in the upper derma and epidermis are insignificant, and the sweat and sebaceous glands, hair follicles and blood vessels are normal. The so-called xanthoma cell of true xanthoma has not been found, and Bodin³ alone has found the giant cells, called Bodin cells, about the lesions in the region of the blood vessels. Bodin lays considerable stress on the cells, describing them in detail, including the fact that some of them contained fragments of elastic fibers. Their presence in his case suggests the rôle of the foreign body giant cell so often seen in the processes of degeneration and inflammation.

CLINICAL CASE REPORT

History.—Mrs. A. E., an American woman of German parentage, 39 years old, was born in New York City and had never left the country. Her father had died at the age of 53 years, probably of kidney complications, the result of chronic alcoholism. Her mother was well. Neither parent had ever shown a skin condition similar to that of the patient. She had three brothers and one sister. None of the brothers, who were all well, have ever shown any evidence of a similar skin disease. The sister, who died at the age of 34 of pulmonary tuberculosis, showed the same condition as the patient. It appeared when she was 4 years old. The skin of the entire circumference of the neck was involved; but the folds, which our patient has had for the last four or five years, were never present in the case of the deceased sister. No other portion of the skin of the sister was ever affected by the disease.

The patient and her sister were the only ones of the known circle of relatives who had shown this particular type of skin disturbance. The patient had a child who was free from any like condition.

Mrs. A. E. had the usual diseases of infancy, and specifically mentions the acute exanthems, measles and scarlet fever, and also diphtheria. At the age of 18 months, an abscess of lymph node in the left axilla was incised. The scar from this procedure is still present.

General Examination.—The patient was a small, slight woman. Her height was 5 feet, 1 inch, and her weight about 99 pounds. She appeared only fairly well nourished. Physical examination revealed that the heart and lungs were apparently sound, and neither in the liver nor other abdominal organs could any abnormalities be detected. Enlarged lymph nodes could not be palpated in the neck, in the axillae or in the inguinal regions.

Roentgen-ray examination of the chest revealed nothing abnormal in the lungs, but did show enlarged mediastinal lymph nodes.

The first urine examination of a casual specimen was reported acid in reaction, clear, and with a specific gravity of 1.021. There were no casts, and the examination for albumin was negative. There was a slight trace of indican. The diacetic acid test was negative, but there was a heavy trace of acetone and a faint trace of sugar.

3. Bodin: Pseudoxanthoma elastique, *Ann. de dermat. et syph.* Ser. 4, 1:1073, 1900 (with histologic cut and illustration of Bodin cells).

Another specimen of urine was examined after the patient had been asked to abstain from eating candy, in which she had frequently indulged, having been employed in a candy factory. This and later specimens were negative for sugar. The Wassermann reaction was negative.

The blood chemistry was:

Alkaline reserve	43	(Normal 50-55)
Creatinin mg. per 100 c.c.....	2.3	(Normal 1-2)
Sugar mg. per 100 c.c.....	166	(Normal 75-120)
Urea	13	(Normal 11-15)
Uric acid	1.1	(Normal 1-2)

From this it can be seen that the laboratory tests were negative. The slight increase in the blood sugar and the slight trace of sugar found in the first specimen of urine were due to an excessive intake of sugar.

Skin Condition.—The lesions of the skin under discussion first appeared on the neck of the patient when she was 4 years old. The other areas, which now show the affection, appeared in an unnoted order. The patient was certain that the various types of eruption which she had, and which will later be described, had always appeared as they did when she presented herself, except that the wrinkling which was so evident on the neck and on the axillary surfaces of the arms, was supposed to have been present only for the last four or five years. The lesions had never been troublesome, and the patient came for treatment only for cosmetic purposes.

The lesions involved the skin of the entire circumference of the neck, the inner third of both clavicular regions, the suprasternal notch, the axillae and the cubital flexures extending from the middle of the arm to the middle of the forearm. No lesions could be found on the face, the hairy scalp, the lower abdomen, the inguinal regions or the popliteal spaces.

Types of Lesion.—For clarity of description, and in order to convey a comprehensive conception of the case, three types of lesion must first be described in detail. Whether or not there is any relation between these three, whether they are stages or phases one of the other, or whether they are independent characters of the disease, remains a matter for speculation.

The first type of lesion is from $\frac{1}{64}$ to $\frac{1}{16}$ inch in diameter. It is a circumscribed, elevated, smooth, papular, infiltration of fresh butter yellowish hue. These lesions are irregular in outline, with straight rather than curved periphery. Some of the lesions are round or irregularly oval. The sides of the papule may be straight instead of sloping. These lesions may be isolated, especially at the borders of the other lesions at the neck. They may be grouped in twos and threes, or two or three may be confluent, that is, have one border in common, but the individual character of each is not completely lost in the combination. Some lesions of the neck of this type appear to be arranged in irregular lines that run in all directions, transversely, longitudinally and diagonally, and the lines appear to run together frequently, forming a sort of network effect. The skin between these lesions is slightly grayish pink in color, and the capillaries appear slightly dilated and telangiectatic. This skin appears thinned also.

The second type of lesion is a raised plaque, perhaps $\frac{1}{16}$ or $\frac{1}{8}$ inch above the surface of the normal skin. The plaques are of various areas from half an inch to a side to 2 or 3 inches. The borders of the plaques are sloping, regular and sharp in some places with a fading off in others, at times into areas of normal skin and at other times into small areas of the individual lesions such as described in the foregoing, that is, the small lesions appear at the borders of the

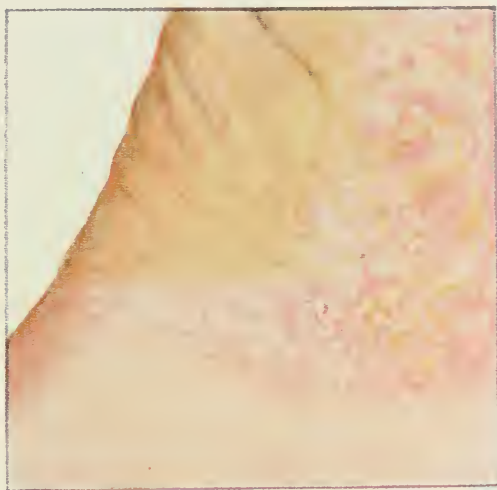


Fig. 1.—Pseudoxanthoma elasticum (slightly enlarged) showing the individual lesions and part of one raised plaque from side of neck. This illustration was made by Alfred Feinberg.

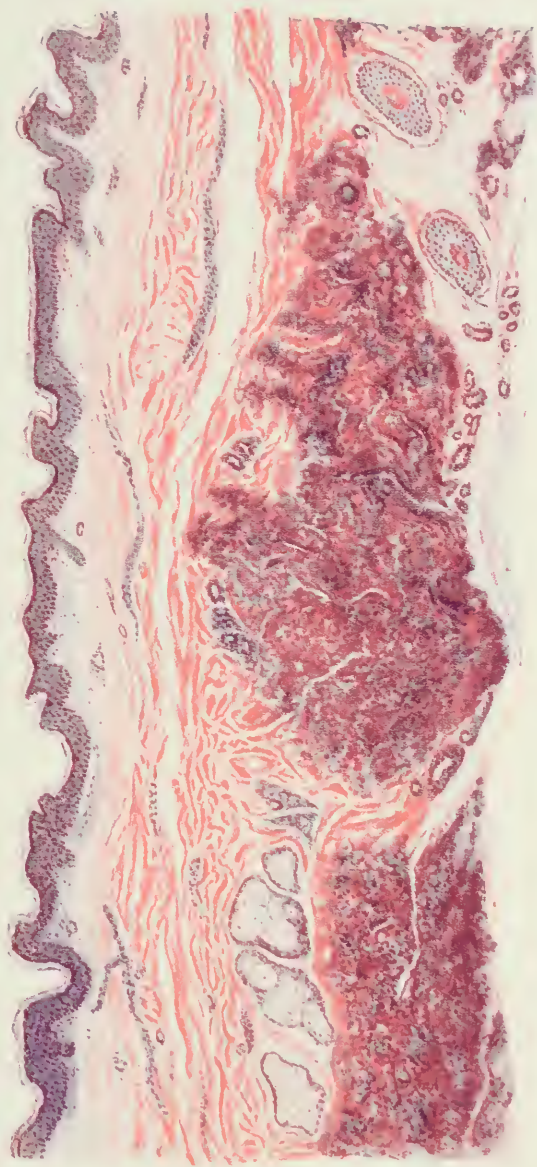


Fig. 2.—Pseudoxanthoma elasticum (New York Skin and Cancer Hospital Path. No. 5,444). Low power colored drawing (by Eva Carrington). Hematoxylin stain. The degenerated elastic tissue stained purple, together with the intermingled collagen fibers showing basic staining, form the deeply stained masses in the lower derma. In normal skin the elastic fibers would be invisible with this stain and the deep derma would only show the collagen fibers stained red with eosin as seen in this drawing in the upper derma.



Fig. 3.—Pseudoxanthoma elasticum (New York Skin and Cancer Hospital Path. No. 5,444). Low power colored drawing (by Alfred Feinberg). Weigert's hematoxylin nerve tissue stain. This stain has a selective action for the degenerated elastic fibers in the middle and deep derma which stand out as distinct black masses. The normal elastic tissue is not shown by this stain.

larger plaques. The surface of the plaque is not smooth, but roughened and moderately granular. One may conceive rather than perceive, the preexisting small lesions in the plaque.

The third type of lesion is limited to the flexor surface of the arms. The lesion is a flattened plaque, not perceptibly raised above the normal skin, and of a lighter tawny yellow. This lesion could be readily overlooked during a casual and superficial examination of the patient. The surface is smooth, except for the depressions of the mouths of follicles which are more prominent in this type of plaque than in the raised plaque.

To the touch, the lesions of the first type are exceedingly soft individually, but the skin surface from which they rise is harder than normal, more leathery than ordinary skin and gives a greater resistance when picked up between the fingers. The raised plaques are doughy and nonelastic. The flat plaques of the flexures of the arms are not infiltrated.

In the neck, the creases are extremely exaggerated and more or less permanent. The slightest movement of the neck increases the depth and intensity of the creases. When the patient has her head at rest in the normal position, the creases are still to be seen, but not so readily as when the head is rotated laterally. No matter how much effort is made to tilt the chin upward, the skin of the anterior portion of the neck is never at a stretch—there is always a redundancy. In the axillae, this feature of the disease is very noticeable, and with the arms at right angles to the body the skin of the axillae hangs pendulous and in folds.

No areas of the skin surface other than those given as the site of the disease process shows any abnormality of texture, nor is there any exaggeration of the wrinkles such as any woman of 39 is likely to have. The patient had several pigmented moles.

The distribution of the three types of lesions is interesting. On the anterior surface of the neck, and encroaching a little toward the left, there is a preponderance of the isolated individual lesions of Type 1. On the sides of the neck, and covering the posterior aspect entirely are the raised plaques of Type 2. These two types are present together in the axillae, the apex of the axilla having more of the plaques, while the limits of the axilla have the individual lesions. As mentioned before, the plaques of Type 3 are present alone on the flexures of the arms and forearms.

It is worthy of note that the scar in the left axilla shows no lesions of the three types described.

Histologic Changes.—(Report of Dr. D. S. D. Jessup of the New York Skin and Cancer Hospital, Path. No. 5444). Tissue was excised from a lesion of the arm near the axilla. Paraffin sections were made and stained by hematoxylin-eosin, Verhoeff's, and Weigert's elastic tissue stains, Mallory's anilin blue stain, Van Gieson's picric acid fuchsin, Unna's polychrome methylene blue stains and Weigert's hematoxylin nerve tissue stain.

The epidermis is thin with a loss of the pegs, and it is thrown up into folds by prolongations of the derma. There are a few scattered pigmented cells in the epidermis and upper papillary portions of the derma and a few mast cells. There is no cellular exudate and in other respects these regions are normal. The noteworthy changes are in the middle and deeper portions of the derma and are most strikingly brought out by the hematoxylin-eosin stain. Here, instead of the normal bundles of collagen fibers stained red with the eosin, there are irregular islands or masses of deep purple staining tissue. They take the stain seen in calcareous deposits. Examined under the high power, there is

a tangled network of short fibers, fine or coarse, and appearing as granules or short rods when in transverse or oblique section. The lesion is in bands parallel to the surface of the skin and in some places is broad enough to occupy the whole middle and lower derma down to the subcutaneous fat. The surrounding collagen fibers stain normally, but those interspersed in the purple staining areas show varying degrees of the basic stain such as is seen in basic degeneration. This is brought out by the Verhoeff and Weigert elastic tissue stains in which there is sharp contrast between the deeply stained elastin and less deeply stained elacin and the clear red of the collagen, which with these two stains—does not show basic degeneration. The affinity of the elastic fibers for the basic stain in the hematoxylin-eosin sections is characteristic of degenerating elastic tissue so that they are not seen in the normal derma with this stain.

With Unna's polychrome methylene blue the degenerating elastic fibers appear as glistening unstained granules with pale blue stain of the collagen in the lesion. In the Van Gieson sections the elacin fibers appear as yellow granular clumps. The collagen stains a paler pink than normal and does not give the yellow reactions seen in colloid milium with this stain. Mallory's anilin blue shows a varying intensity of the blue of the collagen fibers in the lesions as though



Fig. 4.—Pseudoxanthoma elasticum, showing the character of the skin of the neck and the left axilla. The increased nature of the folds, and the almost pendulous reduplication should be noted.

there were some degeneration and loss of staining power. The elastic fibers are in granular masses stained pink or orange. With a view to determining whether the nerve fibers were altered, Weigert's hematoxylin nerve tissue stain was employed. No changes were noted in the nerve fibers, but the stain brought out most strikingly the degenerated elastic fibers in the deep derma. The stain has a selective action for elacin, staining the swollen fibers and granules a deep black, but the normal elastin is unstained, and the rest of the tissue in the section, stained pale brown, is in marked contrast to the black elacin.

There are no changes from normal in the blood vessels, sweat and sebaceous glands, and in the tissue sectioned the hair follicles do not show any of the changes that might be expected from the clinical appearance of some of the lesions. There are no cells of the type seen in true xanthoma and no giant cells. The various stains lead to the conclusion that the lesion is a degeneration of the elastic tissue in the deeper portion of the derma and a moderate change

also in the collagen in the lesions. The elastic fibers compared with those of normal skin are swollen and irregular in outline and have lost their normal reaction to the various stains showing the changes of elacin or degenerated elastin. At the edge, the normal elastic fibers appear to be continuous with the degenerated ones.

COMMENT

In our opinion, based on the clinical aspects alone, the primary lesion of pseudoxanthoma elasticum is the individual papule, designated as Type 1. By confluence, the raised plaque of Type 2 is formed. The



Fig. 5.—Case of pseudoxanthoma elasticum observed in the service of Dr. A. S. Clark, New York Skin and Cancer Hospital.

larger plaques of the raised type, as seen on the back of the neck, seem to be due to the confluence of smaller plaques, and this appeals to us as accounting for the granular appearance of the larger plaques. The presence of individual lesions at the borders of the plaques seems to show a progressive development where these are found, namely, on the neck and in the axillae. On the other hand, the plaque of so-called Type 3 seems to have been formed from lesions developing at one

time. The absence of individual lesions at the border of the last type of plaque seems to sustain this view.

Unfortunately, the patient did not permit a sufficient number of biopsy examinations to add any histologic evidence to this theory. We must say that during the period that the patient was under our observation, from April, 1920, to the date of the present writing, there has been no visible change in the clinical manifestation.

REVIEW OF THE LITERATURE

The following review of the literature consists of rather full abstracts of case reports, with clinical and histologic data. Important generalizations, discussions, etc. are not included under this heading, but will be found in another section of this paper.

*Balzer's*¹ Case.—Balzer reported the case of a man, aged 49, a mason, admitted to the Hospital Saint Louis on Oct. 26, 1882, with pulmonary tuberculosis. According to his statements, his mother had died as a result of chronic lung disease. The patient had had intermittent fever during his military service. Since that time he had been in good health until he commenced to cough in April, 1881. He stated positively that he had never had jaundice.

During the past year he had had several small hemorrhages and had become progressively weaker, so that he had been unable to work for seven months. He had slightly improved by treatment. For several months he had suffered from headache coming on in the morning but ceasing during the day. Quinin sulphate and sodium salicylate relieved these headaches to a great extent. During the month of November, he had had severe chills several times a week, with a rise of temperature to 39.5 C. Physical examination showed a cavity at the right apex with souffles; at the left apex there were subcrepitant râles and disseminated moist râles over the entire chest, predominating on the right. There were no pathologic heart signs. Loss of appetite and persistent diarrhea were symptoms.

Numerous xanthelasmatic plaques covered the surface of the body, which the patient stated he had noticed since childhood. The condition had been more noticeable when he was young. The plaques were like those of xanthelasma planum, pale yellow in color, visible especially on pressure. They were irregularly distributed, and very variable in size, varying from 1 sq. mm. to 1 sq. cm. They were especially numerous around the navel, where they were slightly raised. The plaques were less numerous on the chest and on the back. They were also numerous on the neck, especially at the back; they followed the folds of the skin, and their longest axis lay parallel with these folds. The patient's face was yellow, but there were no real signs of jaundice in the conjunctivae or in the urine. On the limbs the yellow plaques were especially numerous in the folds of the elbow and axillae, less so in the groin and at the knees.

The diarrhea resisted all treatment, and the patient grew rapidly weak and cachectic. He died on November 29.

Necropsy examination showed the lungs covered with tubercles and fibro-caseous masses; there were numerous adhesions, and cavities in both apexes. The liver was large and of the color of yellow ochre. Subsequent microscopic examination showed simply a fatty liver without any special lesion. The

kidneys were slightly sclerotic. The spleen was normal. The most interesting changes were seen in the heart. The right auricle showed a light yellow color on its inner surface without any evident thickening of the endocardium. This yellow coloring was visible throughout the columnae carneae, but not on their posterior aspect and not in the auricle. This coloration resembled somewhat that of the plaques in sclerosis of the endocardium, but the appearance of the membrane was duller and more opaque than in sclerosis. It could also be seen, though less clearly, on the pericardium.

Careful histologic examination of the xanthelasmatic plaques of the skin and the heart were made. After hardening in absolute alcohol sections were prepared in various ways: (1) staining with picrocarmine and mounted in glycerin; (2) staining with eosin dissolved in alcohol, and mounted in a potash solution of from 10 to 40 per cent.; (3) other sections first placed in potash solution were later stained with methylene blue or picrocarmin and then mounted in glycerin. When fat was present in sufficient quantities to interfere with the examination, sections were treated with ether, essence of clove and absolute alcohol before being stained.

The sections treated with eosin and 40 per cent. potash solution gave the best results. It is advisable, however, to use several methods and to make several series of examinations.

With the low-power of the microscope, several plaques were seen in a single section, usually lying immediately beneath the pars papillaris and separated from the epidermis by a layer of normal tissue of variable thickness. The plaques varied greatly in size and shape, some being long and some round. They were formed of fibrous tissue which the picrocarmin colored rose and of a material that picric acid colored greenish yellow. Under the high power it was seen that this material was the elastic tissue which was remarkably altered. The connective tissue was thickened and formed a fascicle enclosing the irregularly shaped plaques, thus outlining the space filled by this altered elastic tissue. The elastic tissue was increased. Its fibers appeared more numerous than normal because they were hypertrophied, split and segmented transversely. Sometimes their fragments were entirely broken off so that they looked like irregular crystals; sometimes they remained end to end resembling mycelium hyphae. The change commenced by a tumefaction of the fibers, which then split and finally separated transversely. The fragments usually remained close together following the direction of the original fibers. Sometimes these fragments were in a continuous line with normal elastic fibers. The size and shape of these fragments were variable, ranging from segments similar to crystals to small elastic grains. More rarely the splitting took place lengthwise; in this case their histochemical composition appeared to be altered, as they did not stain well with picric acid; and eosin and potassium gave them a violet red shade deeper than normal fibers. Sometimes, on the contrary, they resisted all stains and remained dull and pale. There was little fat and few xanthelasmatic cells. In some sections the elastic fibers were entirely destroyed, leaving compact masses of irregular opaque granulations. The process was everywhere the same—in the small disseminated plaques and the larger plaques whether superficial or deep in the skin, and in the plaques of the heart walls.

Darier's² Case.—Darier reported the case of a man, aged 42 years, under the title of pseudoxanthome elastique. The family history was not important. The patient had had typhoid at the age of 23; then alcoholic gastritis with repeated hematemesis and jaundice; also malaria. There were signs of indura-

tion, probably tuberculous, at the apexes of both lungs. The blood was normal. The urine did not contain sugar.

When 26 years old, he had noticed a livid spot in the folds of the elbow joint, which itched slightly. This soon became yellow and had remained so since that time. Other regions were attacked soon after, and the condition had progressed steadily. At the time of the report it extended symmetrically along the skin folds of the trunk and of the large joints of the limbs—that is to say, the neck and clavicular region, the elbows, the abdomen below the navel, the under surface of the penis, the inguinofemoral region, between the buttocks and the posterior surface of the knees. The lesions consisted of large spots or plaques resembling xanthoma, of a yellowish café au lait color. The plaque on the elbow measured 5 by 10 cm. On close examination it was evident that the plaques were formed by the confluence of small miliary spots of a creamy white color, arising from a reticular base of violet or lilac shade. The skin in the vicinity was tender to the touch, slightly doughy in consistency, relaxed and less elastic than normal. Around the plaques were small yellow papules, surrounded by an areola, with a pigmented follicular orifice in the center, similar to "diabetic xanthoma." The back, the breast, the extensor surface of the limbs, the hands and the feet showed no lesions. The head was not much affected, but there was a small yellowish spot on the palpebral commissure of both eyes, and spots of a dull white, confluent at certain points with a vascular base, on the mucosa of both lips and on the inner surface of the cheeks.

Histologic examination was made of specimens taken from different sites, prepared with different reagents, and different stains were used on the sections. The technic giving the best results was orceinic acid for study of the section as a whole, and eosin and potash in 40 per cent. solution, or osmic acid and safranin, with decoloration by tannin, for the study of details.

With low power microscope, it was evident that the lesions were made up of elastic tissue at the level of the corium. This tissue was augmented more by the enlargement and twisting of the fibers than by a true hypertrophy. In the plaques of the axilla, for example, this alteration of the elastic tissue extended from beneath the pars papillaris to the hypoderm in the form of a continuous layer in which, however, imperfect lobulation could be observed, and a tendency to form round lumps, more or less confluent or separated by healthy fibers. Sections of isolated papules showed alteration of the elastic tissue around a pilosebaceous follicle, which it surrounded like a crown.

With a high power microscope, it could be seen that the elastic tissue fibers were thickened and enlarged and often broken into fragments. These fragments, in the shape of rods or short cylinders, remained in contact, thus resembling chains of large bacilli. More frequently the fibers were swollen and beaded, oddly twisted, with vacuoles and longitudinal fissures. In some cases they had become veritable plaques with a number of vacuoles. In other cases they had completely disintegrated into amorphous masses of clots or granulations. These changes merited the names of elastoclasia or elastorrhexia, by which the author designates them. In a number of ways it was easy to show that these peculiar formations were in direct continuity with the normal elastic fibers, when at a certain point, the normal formation abruptly took on the character of elastorrhexia.

At the same time, these morphologic changes produced some chemical changes in the elastic tissue. The granulations were less resistant to potash, stained less readily with acid stains, but slightly with basic dyes. They stained violet with hematin.

The connective tissue, as shown in different preparations, was not noticeably sclerotic in the neighborhood of the elastorrhexia; the cells were slightly increased in number next to the altered elastic fibers; some connective tissue cells showed granulated protoplasm, but these did not stain with osmic acid and did not resemble in any way xanthoma cells. It is important to point out that xanthoma cells were not found in any of the sections examined.

Bodin's³ Case.—Bodin made a study of a man aged 50 who had entered the hospital of Rennes for bronchitis of several months' duration; there was nothing of interest in his family or personal history. He had been in good health until he began to cough. When he entered the hospital he was thin and weak and had night sweats. Examination of the chest showed signs of tuberculosis in both lungs, especially at the apexes. The character of the sputum confirmed the diagnosis. Digestive troubles were also noted, including loss of appetite and diarrhea, but examination of the liver showed nothing of note, and he had never had jaundice. The urine was normal and did not show sugar. For thirty years the patient had had numerous skin lesions to which he had given no special attention, as they had never given him any trouble and had increased only slightly since they first appeared. The lesions were particularly numerous on the abdomen below the umbilicus, extending symmetrically on each side of the median line, and reaching a size larger than the palm of the hand. The lesions elsewhere were also absolutely symmetrical—in the clavicular region, the axillary region, the inner surface of the arm and the anterosuperior surface of the forearm, and the interior upper surface of the thigh. The lesions were arranged in plaques of more or less regular shape, in the center of which the elements of the dermatosis were seemingly confluent but actually separated by small spaces of normal skin. Toward the edge of the plaque they were separated from each other and gradually diminished in size until at the outer edge they were small punctiform spots. Closer study of the lesions showed that these elements were all similar, pale yellow, sharply defined, varying in size, being oval or rounded, apparently homogenous or slightly granulated. At the surface of the skin, they formed a slight projection which could be easily seen and felt, but the skin around them appeared to be absolutely normal. Palpation revealed no induration and caused no pain.

For histologic examination two pieces were excised from the abdominal lesions, fixed with sublimated acid (formula of Nicolle), then mounted, some sections in paraffin and some in gum, and treated with various stains. Under a low power microscope the lesions were seen to be situated superficially in the derma at the level of the upper part of the reticular layer, above the sweat glands, with which they had no relation. Their upper surface did not reach the papillary layer. In section they were ellipsoid in shape, the long axis being parallel to the cutaneous surface, measuring from 300 to 400 microns on their long diameter, and from 0.4 to 0.6 mm. on their short diameter. At the surface, there were small irregular masses of granulated matter situated between the connective fibers of the derma, which were crowded together around them. Below these lesions the derma was normal; above them the pars papillaris was also normal. The walls of the small vessels were slightly thickened and showed a slight round-cell infiltration. In some places the pars papillaris appeared slightly thinner over these lesions, but the difference was only slight. In the epidermis, this thinning, corresponding to the xanthomatous elements, was more marked, especially in the mucous layer. Subcutaneously the fat globules were abnormal; the fat cells composing them were separated from

each other, and when stained with osmic acid, the fat was seen to have accumulated at one pole. The rest of the cell appeared to be filled by a liquid.

When the xanthomatous lesions were examined under the high power three different elements were found: (1) small masses of granulations, (2) connective tissue, (3) special cell elements, mostly around the vessel walls.

1. The small granulations were made up of tissue which showed the histochemical characteristics of elastic tissue: they stained yellow with picrocarmin; eosin stained them rose; methylene blue and orcein stained them equally well. If, after staining with eosin, the sections were mounted in 40 per cent. potash solution, they kept the rose color of the elastic fibers in the rest of the tissue completely decolorized. They showed, however, a more violet tinge than normal elastic tissue treated with the same stain. The small masses of elastic tissues appeared broken up into irregular crystal-like fragments. The continuity of these fragments with normal elastic fibers was less frequently seen than in Balzer's case, but otherwise their appearance corresponded exactly to the descriptions of Balzer and Darier.

2. Between the masses of elastic tissue fragments, the connective tissue was broken up and crowded around these masses, but it did not appear to be altered in its histologic characteristics, except that there was an increase in the number and size of the connective tissue cells.

3. No xanthomatous cells, such as are typical of true xanthoma, were found, but there were a number of giant, polymorphonuclear cells of variable size and shape. These were found in the vicinity of the vessels, chiefly at the edge of the lesions. There was considerable variation in the morphology of these cells. Many were giant cells of variable size, some as large as 50 by 30 to 45 microns with uniform granular protoplasm and a number of round or oval nuclei. Other giant cells were represented by their nuclei alone or showed little protoplasm. Others showed signs of beginning degeneration—there were some giant cells of irregular outline with nuclei that did not stain normally, some with hyaline degeneration of the protoplasm and others with a degenerating protoplasm which showed staining reactions similar to those of the elastic tissue fragments. On close examination some of the giant cells seemed to be almost completely assimilated by the elastic tissue, with scarcely any nuclei and only a few fragments of the original cell showing marked degeneration; or an elastic tissue fragment might be enclosed completely or partially in a degenerating giant cell.

Von Tannenheim's Case.—Von Tannenheim's case was posthumously reported. He had observed the case of a woman aged 76. She was moribund when she came to the hospital, and no history was obtainable. The lesion was first found at necropsy. The skin in general was pale and slightly pigmented. On the anterior side of both upper arms and thighs and on both sides of the iliac crest were yellowish or opaque infiltrating lesions, irregular in shape, the size of millet seeds, but confluent and forming plaques where most numerous. On section they appeared as dry yellowish white foci in the the cutis, the epidermis appearing unaltered. A few lesions were noted under the skin and on the sides of the thorax.

Necropsy examination revealed in addition: arteriosclerosis, endocarditis, myocarditis, lobular pneumonia, intestinal hemorrhage and senile marasmus.

4. Von Tannenheim: Zur Kenntniss der Pseudoxanthoma elasticum (Darier), Wien. klin. Wchnschr. **14**:1033, 1901 (with two histologic cuts).

Pieces of skin were taken from the upper arm and the thigh for histologic examination, and preserved in alcohol, liquor formaldehydi, Zenker's and Muller's solutions. Sections were mounted in celloidin.

With the lower power unstained sections showed opaque, oval lesions not clearly defined in the upper layers of the corium, the pars papillaris being attenuated and flat. The lesions were separated from the epidermis by apparently normal connective tissue. The oval lesions showed the diameter parallel to the skin surface. They did not extend into the subcutaneous tissue nor to the sweat glands. They appeared to be composed of granulated opaque sections which in places were separated from each other by homogeneous, sometimes swollen connective tissue fibers. When more closely observed this granulated tissue was seen to be in direct continuity with strong, glossy fibers in the surrounding tissue. These fibers, as they entered the lesion, were split up and twisted into knots until they disappeared in the opaque lobules. In some sections these lesions appeared darker and the outlines of the knotted fibers clearer and sharper. The addition of dilute sulphuric acid produced gas bubbles and calcium sulphate crystals, indicating calcification and the deposition of carbonate of lime.

On staining with hematoxylin-eosin, the opaque portions of the lesion were seen to be composed of red staining fibers or coils, or spirally twisted bands, which under the high power appeared as granular, curved sometimes glistening masses. Between these masses the connective tissue was sometimes normal in appearance, but sometimes the fibers were homogeneous, swollen and also stained red.

The pars papillaris of the corium, as noted in the foregoing, was much thinned; otherwise the skin showed little change.

Every staining method to demonstrate elastic tissue showed that these lesions give the same reaction. The opaque coil-like parts of the lesions stained somewhat lighter than normal elastic tissue (with orcein, brownish red or light brown, with the Weigert stain, blue-gray), but they were in direct continuity with the elastic fibers of the surrounding tissue. Occasionally similarly altered elastic fibers were seen in the deeper layers of the cutis.

With picric acid contrast staining, the coils and granular masses of the lesions showed a yellow color, or occasionally remained a light brown, like the other elastic fibers of the cutis. With a combination of the elastic tissue skin and the van Gieson stain the connective tissue fibers in the center of the lesions usually stained only a light or yellowish red, while the connective tissue at the periphery was fuchsin red. With van Gieson stain alone the lesions described stained yellow, like elastic tissue; the connective tissue fibers of the cutis stained in different shades of red.

In the layer directly beneath the epidermis, in the midst of the normal tissue, was a stratum, staining intensively with elastin stains, which was composed of variously shaped bodies, sometimes U-shaped, sometimes coiled or spiral. In many cases these were directly continuous with the fine elastic fibers of the surrounding tissue; in other cases they showed no relationship to these fibers, but on section looked like enlarged and misshaped elastic fibers.

*Dubendorfer's*⁵ Case.—Dubendorfer reported the following case in a 7-year old boy who came for treatment for a slight psoriasis. In the left upper gluteal region there were several irregular rounded spots the size of the palm of the

5. Dubendorfer: Ueber "Pseudoxanthoma elasticum" und "Colloide Degeneration in Narben," Arch. f. Dermat. u. Syph. **64**:175, 1903 (one colored plate of histology).

hand and more numerous raised bands and spots. The latter were on the average 1 cm. long and from 0.25 to 0.5 cm. wide. The surface structure of the skin was normal. No psoriasis lesions were found in this region. The bands were only slightly raised. They were sometimes parallel to each other, sometimes confluent, forming a widemeshed network. When the surrounding skin was hyperemic, they were often difficult to distinguish clearly. They disappeared into the deeper layers of the cutis, showing a yellowish tinge through the cutis. On pressure, a slight elevation under the cutis was felt and on heavier pressure a slight resistance was noticeable. There were no subjective symptoms. The lesions did not change in the several weeks that the patient was under observation. The yellowish color of these lesions was the most noticeable symptom.

An elliptical piece was cut across the long axis of one of the bands, including normal tissue on both sides, fixed in absolute alcohol and mounted in paraffin. With ordinary nuclear stains, only a few changes could be seen. The epithelium and the pars papillaris were normal. Around the vessels, especially around the follicles, there was slight infiltration, mostly of mononuclear leukocytes. There were no signs of inflammation. Much more evident changes were noted with elastic tissue stains, both with orcein and Weigert's stain. With a low power, sharply circumscribed lesions were seen in which the deeply stained elastic tissue fibers appeared in large numbers and in peculiar arrangement; these lesions were situated in the middle and deep layers of the cutis, reaching nearly to the subcutaneous tissue. They had no relation with the vessels, the follicles, or the sweat glands. The cutis lying between the lesions appeared absolutely normal as regards both the elastic and the collagenic tissue.

With the high power microscope the center of these lesions was shown to be formed of deeply stained elastic tissue—no longer in normal fibers, but either in numerous fragments or in bands of unusual width and irregular contour. Between these, only collagen tissue was seen. On closer examination it was seen that the intensity of the stain varied, and in some locations, small dark nuclei were seen within the bands. On the periphery of the lesions it could be seen that these fragments and bands were the continuation of elastic fibers, which were, however, swollen and irregular in outline. In some instances, however, the transition to normal elastic fibers appeared to be more sudden. Outside the lesions, also, the elastic fibers appeared somewhat abnormal, less sharply outlined than usual, irregular and knobby in outline and splitting at the ends.

Staining showed the collagen tissue to be normal.

*Werther's*⁶ Case.—Werther reported the case of a woman aged 28, who stated that two of her sisters had had the same kind of skin lesions. The patient had chronic stomach trouble, for which she was dieting regularly. She appeared pale and weak; her appetite was poor. The lungs were normal. The urine showed neither sugar nor albumin. The skin lesions were most numerous around the neck, extending from the hair line downward and forward to the clavicle, and behind to the spines of the scapulae. Lesions were also found in the anterior axillary folds and at the elbow joint. The lesions were raised from 2 to 3 mm. above the skin surface. The color was that of ivory, with a slightly bluish tinge. On the neck the lesions were confluent, forming an irregular network. On the edges of this lesion and elsewhere where the lesions were less marked there were separate rounded papules. The surface was smooth, and

6. Werther: Ueber Pseudoxanthoma elasticum, Arch. f. Dermat. u. Syph. 69:23, 1904 (one clinical stereoscopic picture and two colored histologic plates).

the consistency soft. The skin surrounding these papules had a peculiar glistening appearance. The skin lacked the normal elasticity, especially around the neck lesions. There was only a mild itching. The lesions were first noted when the patient was 16 years old. They had increased gradually since that time. During the three months that the patient was under observation no change could be noted.

A piece was removed from the edge of one of the lesions. Sections were prepared as follows: (1) in glycerine, unstained; (2) stained with hematoxylin and eosin; (3) van Gieson stain; (4) Wiegert stain; (5) Unna-Taenzer stain-orcein and methylene blue; (6) elastic tissue stain by Unna's method (orcein, polychrome methylene blue and orange-tannin solution).

The examination showed a normal epidermis, and the pars papillaris flattened or stretched. The subpapillary blood vessels were prominent because surrounded by new connective tissue. The connective tissue bundles of the derma immediately beneath the epidermis showed their regular normal arrangement. The elastic fibers showed their normal fineness, running horizontally in the lower strata and extending upward into the epidermis.

In the layers of the derma, there was a region of the abnormal structure evident even in the unstained sections. This region was sharply defined and never extended into the subcutaneous tissue. This region, in the unstained preparation, was filled with irregular granulated, knotted bundles, which, with the lower power lens, were seen to be closely packed together and showed an irregular refraction of light. In this region lay the characteristic lesions which clinically appeared as yellowish raised papules. This region stained intensively with eosin and showed fewer interstices than the surrounding layers. The connective tissue nuclei were increased. With the high power lens it was seen that the eosin stained collagen bundles were irregular in arrangement and in outline. Between the collagen bundles was a granulated mass that stained less intensively with eosin and in some sections diffusely with hematoxylin. The exact nature of this mass could not be determined with these stains.

With the van Gieson stain and the low power microscope the actual lesion showed larger spaces between the collagen bundles, which stained fuchsin red, than the region around them. They were seen to be filled with material that stained with picric acid so that the yellow overshadowed the red. With the high power lens this yellow tissue was seen to be, not homogeneous, but granular or cloudy, and occasionally showed nuclear staining properties (brown in this case), hence basophilic characteristics.

It is evident that the elastic fibers, which stained slightly with eosin and with the picric acid of the van Gieson stain, were chiefly responsible for the clinical lesions, and that this tissue differed somewhat in chemical and physical characteristics from the normal. The connective tissue was also involved but to a lesser degree.

The specific elastic tissue stains, according to the Weigert and Unna methods, showed the changes more clearly. With a low power lens, the elastic fibers above and below the lesion were seen to be as fine as normal, of even outline, and regular arrangement. In the affected region, however, a normal regular fiber was rarely seen. Here there was an irregular arrangement of swollen, granular coils. As a rule, this tissue stained less intensively with orcein than normal elastic tissue. With the Weigert stain the difference was less marked.

With a more powerful microscope, with either stain, the transition stage between normal and abnormal tissue was more clearly seen. The normal fibers first became thicker and undulating in outline, with numerous constrictions

though without actual segmentation. Occasionally, they showed a segment that did not stain—a picture that resembled a mycelium. The arrangement of these fibers also was more irregular than the normal, and the ends were either brushlike or knotted. Here also some nuclear staining tissue was evident. Between the fibers and the fiber fragments were numerous cells which were of the general type of connective tissue cells, though varying somewhat from the normal. With polychrome methylene blue, mast cells were seen in the lesions and the immediate surrounding region. There were no giant cells. The use of the Unna "elastic-elagin" stain showed a blue reaction in the diseased tissue, while normal tissue showed a light brown orcein color. The change from staining to nonstaining segments was also shown.

Gutmann's Case.—Gutmann had under his care a woman 23½ years old, with chlorosis and constitutional syphilis. Her face was much freckled and her neck somewhat so. In addition, a skin affection was noted on the neck, consisting of whitish or yellowish slightly raised plaques, over which lay the normal epidermis. They felt harder than the normal skin. Where the lesions were most numerous, they were arranged in rows, sometimes forming a narrow network, in the interstices of which were slightly livid fossulae. The most numerous lesions were on the sides of the neck, extending upward and backward to the hair. Lesions were also noted in front on the throat, though less numerous. The patient stated that these lesions had been noticed since childhood (as long as she could remember) and that a sister and a brother had had a similar affection, also since childhood. She could not say whether the parents or any other members of the family had been affected.

Microscopic examination showed the following: The epidermis was entirely normal. The pars papillaris showed many yellowish, granular cells, and free pigment, also cellular infiltration, especially around the vessels, mostly lymphocytes. Many mast cells were noted in the pars papillaris and also in the adjacent parts of the cutis. In the cutis, the cellular infiltration was less marked, the collagen tissue and the elastic fibers were normal in the pars papillaris and the adjacent section of the cutis. The middle and deep layers of the cutis, with nuclear stain, and sometimes with hematoxylin, were seen to be filled with bluish violet coils and clumps (sections fixed in absolute alcohol). The pathologic process was sharply separated from the upper layer of the cutis above and from the subcutaneous tissue below, reaching nearly to the level of the sweat glands. In some cases the lesion was related to a hair follicle or sebaceous gland in such a way that a typical section of a single lesion was a rectangle with its long side parallel to the subcutaneous tissue and its short side formed by the follicle. The follicles were entirely normal, except for occasional cellular infiltration. Sections of the bandlike lesions showed a pathologic process covering the length of an entire section of the deeper layers of the cutis and about three fourths of its width. Staining with the Weigert and the Unna-Taenzer stains showed that this tissue was made up of altered elastic fibers, which stained somewhat less intensively than normal fibers. The fibers had become irregular masses and coils. Sometimes they appeared widened and spiral or corkscrew-like; sometimes a narrow band that stained a dark brown bordered a gray or light brown center, filled with numerous dark staining nuclei. Often one part of a fiber would show a dark stain, the next a lighter shade, or a fiber would be repeatedly segmented transversely. Sometimes the

7. Gutmann: Ueber Pseudoxanthoma elasticum (Darier), *Arch. f. Dermat. u. Syph.* **75**:318, 1905 (one colored histologic plate).

end of a fiber would be knotted and sometimes brushlike. On the periphery of the lesion, transition forms of the elastic fibers could be demonstrated, showing clearly the change from the normal to the pathologic type. The elacin reaction was negative. In sections fixed in alcohol and stained with the van Gieson stain, the pathologic elastic fibers sometimes showed a peculiar brown violet color.

Collagen tissue was plentiful in the lesions. The trabeculae were somewhat thicker and coarser than usual, otherwise the specimen was normal both in color and in staining reactions.

Cellular infiltration was only occasionally seen in the plaque, and then only around the vessels or the sweat glands. In some sections there was a noticeable increase in connective tissue cells and also scattered giant cells in considerable numbers. Their relation to the altered elastic fibers was not clear. With suitable stains, no fat could be seen within the lesions and naturally no xanthoma cells.

*Dohi's*⁸ Case.—Dohi's patient was a woman aged 74 years. In her youth she had had acne of the face. In later years, she had had an epithelioma of the nose between the two eyebrows, cured by radium. The skin lesions under discussion began many years before—according to the patient's statement—probably twenty years or more. None of her relatives had had any similar lesions. There was no subcutaneous symptoms. Numerous raised lesions, varying in size from that of a pinhead to that of a lentil, round or irregular in outline, were found on the forehead, eyelids, cheeks, upper lip and chin. Their surface was smooth and flat. These lesions showed a xanthoma-like coloring—straw yellow to yellowish brown—and felt harder than the normal skin. Their arrangement was symmetrical. Sometimes they were isolated, sometimes confluent, forming an irregular network. The skin between them appeared normal. The eyelids showed only isolated efflorescences. The scar of the healed epithelioma was visible. There were numerous freckles on the face, hands and forearms.

A piece of the diseased skin was excised from the right cheek, and fixed in absolute alcohol. Sections were mounted in both celloidin and paraffin, and stained in the ordinary way.

The epidermis was normal and only in a few places was it thinner than usual. There was a considerable accumulation of yellowish brown pigment in the basal layer. In the upper layer of the cutis there were a few pigmented round or spindle-shaped cells. The papillae were flattened.

With van Gieson's or Hansen's stains, the cutis appeared to be divided into three distinct layers, which with a low power microscope were sharply defined. With a stronger microscope the transition from one to the other was seen to be more gradual.

The upper zone, nearest the epidermis, showed regular rose colored connective tissue fibers running horizontally. The subpapillary blood vessels and lymph spaces were normal. Next came a wider, less compact zone which was made up of irregular yellowish brown clumps. In this zone were several connective tissue fibers or bundles running horizontally or obliquely, sometimes appearing to connect the upper with the lower zone. The lowest zone was the widest.

8. Dohi: Ueber "Pseudoxanthoma elasticum" und ueber "Kolloide degenera-tion" der Haut, Arch. f. Dermat. u. Syph. **84**:179, 1907 (one histologic plate and two colored figures).

occupying almost two thirds of the entire cutis. The connective tissue bundles usually were horizontal and stained rose red with acid fuchsin. With the stronger power lens, yellowish brown clumps or granular masses were seen between the collagen bundles, especially in the borderline between the middle and the lower zones. The sweat glands and hair follicles lay in the lower zone.

With nuclear stains without contrast staining with acids, blue-violet granular clumps showing affinity for basic stains were seen in the middle zone. The three zones described were less clearly defined than with the van Gieson or Hansen stains. The nuclei of the connective cells were somewhat increased in number in the sharply defined lesions and in the tissue around them. There was slight round cell infiltration in the middle zone of the cutis and a thin layer of round cells around the hair follicles, sweat glands and blood vessels. Mast cells were also increased, especially around the vessels, and in the round cell infiltration of the deeper layer of the cutis.

The findings with the elastic tissue stains, according to the Weigert or Unna-Taenger methods, were much more remarkable. Even with the naked eye, a sharply defined dark area could be seen under the epidermis. With the low power microscope, bandlike irregular granular or clumpy masses were visible in the upper part of the cutis, corresponding to the middle zone in the van Gieson stain preparations. They stained dark brown or almost black with either the Unna-Taenger or Weigert stain, very much like normal elastic fibers, only more intensely in certain regions. This zone covered from a fourth to a half of the cutis and was separated from the epidermis by a narrow, lighter zone. Toward the sides this zone grew smaller; sometimes hair follicles and excretory ducts of the sweat glands formed its boundaries. With a stronger power of the microscope more marked changes were visible. The elastic fibers lost their regular outlines. They were sometimes swollen, sometimes indented, sometimes broken transversely or twined into a network. Often they showed knotty swellings at the end. Sometimes a number of fibers met in a rosary-like formation. The fibers were sometimes straight, sometimes U-shaped, sometimes spiral. Sometimes only a small edge of the fibers stained intensively—black or dark brown, the inner portion being only gray or light brown. Sometimes also there were more or less numerous dark colored nuclei, or vacuole-like lighter spaces. With special elastic tissue stains followed by staining with carmin or polychrome methylene blue, round, spindle-shaped or irregular connective tissue cells, staining normally, and a few mast cells were seen between these altered fibers; with carmin or picric acid stain a small number of red or yellow staining connective tissue bundles were seen. In the upper zone, immediately below the epidermis, which lay over the chief lesions, the elastic fibers were mostly of normal fineness and thickness, running horizontally or with the upper fibers extending upward to the basal cells. Sometimes their number was much diminished, and sometimes they were entirely lacking.

In the lower zone, including the lower half or third of the cutis, the elastic fibers sometimes were parallel to each other, forming bundles, and sometimes woven into a network, but showing normal contour and fineness and normal chemical reactions. By closer observation, it could be seen that the altered fragments extended down into the deeper layer of the cutis to the level of the sweat glands. At the boundary of the lesions the transition from normal elastic fibers to the abnormal fragments could be distinguished, but there was usually a fairly sharp boundary line.

Unna's elacin stain showed a limited number of fiber fragments in the center of the lesions that stained blue or red. Otherwise this stain gave no reaction.

The collagen tissue in the lesions was diminished and atrophied, but its staining reaction and its relation to the elastic tissue masses were normal. It stained well with fuchsin or eosin.

Neither giant cells nor hyaline degeneration was seen. The vessels of the cutis showed no degeneration or thickening of the walls, but occasionally the capillaries showed projecting endothelium in the lumen.

*Little's*⁹ Case.—Little reported a case of pseudoxanthoma elasticum of Balzer in a woman aged 56 years. The eruption consisted of meshlike patches of buff-colored infiltration, lumpy in some places, in others linear and hardly at all raised from the surface; the whole of the neck was occupied by the eruption, but it was especially marked at the sides. The face was entirely free. Small patches of the same type were present in the flexures of the elbow. The condition had persisted for more than twenty years, and there were no symptoms in connection with it. The patient had never had jaundice or liver troubles.

The exhibitor had had two cases, of much more limited distribution of pseudoxanthoma elasticum, in which a biopsy had corroborated the diagnosis; this had not been obtainable in the present instance, but the clinical similarity of the case now shown with these two made this diagnosis more than probable. In Brocq's recent treatise the statement was made that only four cases had hitherto been recorded: one by Balzer, one by Chauffard and Darier, one by Bodin, and one by Werther. This remained, therefore, one of the rarest of skin diseases; but probably the difficulty of diagnosis without a biopsy and the impossibility of obtaining this in many instances added to the obscurity of the disease and the rarity of its identification.

*Bosellini's*¹⁰ Case.—Bosellini reported a case in a woman aged 45 years. There was no history of past disease. According to the patient, the present skin lesions were six or seven years old; the disease had begun as two or three spots on the forehead, and had advanced slowly. At the time of the examination, the dermatosis covered the entire width of the forehead and extended slightly over the roof of the nose and over the cheeks. The elements were symmetrically arranged raised lesions, the size varying from that of a millet seed to that of a hemp seed, lying in racemose groups, and resembling herpes. They were very close together, but always separated by regular grooves. The small groups were found in the folds of the forehead; the grooves within these groups ran horizontally. Vertical grooves with normal skin divided the groups from each other. The elements were smooth, glossy and dark brown or lead color. There was no inflammatory reaction and no desquamation. The dermatosis was also found on both hands, following the radial side of the index finger and the ulnar side of the thumb in a continuous line. Here the individual elements were not so definitely separated and the lesions resembled nevus-like bands.

A small piece of skin from the right side of the forehead was excised, fixed in alcohol and Zenker's fluid, and mounted in paraffin. Several common stains were used with the different sections—for the normal elastic tissue, orcein; for the altered elastic tissue, Unna's polychrome methylene blue and tannin; for the collagen, orange-tannin. In addition to these stains, other nuclear stains were used, especially van Gieson's and Pappenheim's.

The epidermis of the individual lesions, as well as the grooves between them, appeared normal, except that the layers over the lesions were fewer in number.

9. Little: Case Presentation, Brit. J. Dermat. **20**:194, 1908 (author mentions having had two other cases).

10. Bosellini: Pseudoxanthoma elasticum, Arch. f. Dermat. u. Syph. **95**:1, 1909.

There was an abundance of pigment in the basal layer and also in the layer above it; also some vacuolation of the basal layer with displacement of the malpighian cells.

The papillae had disappeared from the pars papillaris, leaving only a connective tissue layer. The staining reactions of the collagen and the elastic fibers of this layer were normal. The layer below the pars papillaris showed no special characteristics and was, in fact, largely absorbed by the latter.

The greatest change was seen in the middle layer of the cutis. With the low power microscope, numerous round foci were seen extending upward. They were imbedded in a diffusely altered tissue, the pathologic changes in both being of much the same character. The elastic tissue in this layer was unusually plentiful between the collagen bundles, and showed a marked basophilic reaction. This made a clear demarcation between the middle and the deep layer of the cutis. The elastic tissue of the deep layer showed an intensive reaction to the orcein stain, but the elastic fibers of the middle layer stained only slightly. If thionin was added to the orcein to produce a nuclear stain, the elastic tissue of the middle layer showed a marked basophilic reaction, which was also obtained with methylene blue and tannin, while these stains gave no reaction in the elastic tissue of the deep layers of the cutis or of the pars papillaris. The elacin showed similar reactions. The collagen bundles were entirely normal in morphology, arrangement and staining reactions.

Considering the single foci, it was evident that they were not all alike. The smallest were composed of a thick feltwork of regular, well developed, clearly defined elastic fibers, with a basophilic reaction. The upper part of these lesions was more compact than the lower, where the fibers showed their continuity with the basophilic fibers of the surrounding cutis. The collagen in these elastic coils was somewhat reduced. There were few connective tissue cells.

Besides these small elastoma, there were larger round or oval lesions in which the elastic tissue predominated, and still larger and more developed lesions composed of collagen chiefly, with a trace of elastin. Above these lesions was a lymph space which separated them almost completely from the pars papillaris. Around the lesions were numerous mast cells, and around the blood vessels considerable cellular infiltration was present but no sign of inflammation.

With the Zenker stain, the lesions showed no special characteristics, but were clearly brought out. With a stain combining polychrome methylene blue, orange and orcein, it could be clearly seen how the elastic fibers were broken up between the collagen bundles, showing granular degeneration, and how the collagen without infiltrating them, gradually covered them.

*Pinkus'*¹¹ *Case*.—At a meeting of the Berlin dermatologische Gesellschaft, March 8, 1910, Pinkus presented the case of a woman, 53 years old, with lesions of pseudoxanthoma elasticum similar in extent to those in the cases of Darier and others. The axillae, the elbows, the region of the navel, the inguinal folds and the neighboring parts of the trunk and the thighs, and, to a lesser extent, the knees, showed lesions. Around the neck, like a band, was a scarred area with contracted skin, in which were the yellow papules of pseudoxanthoma. The folds of skin at the axillae and the groin were exaggerated, and the skin was leathery. The patient was very thin and appeared as if her skin was too large for her. Microscopically the yellow papules contained disintegrating elastic

11. Pinkus; Case Report, Arch. f. Dermat. u. Syph. **104**:94, 1910.

fibers of poor staining reaction, appearing as if only a sheath (and not always intact) was left from which the elastic contents had been extracted.

*Little and Sequeira's*¹² *Case*.—Little and Sequeira reported a case of pseudoxanthoma elasticum. The patient had been seen by Dr. Little at St. Mary's Hospital about seven years ago, when she was about 12 years of age, and was subsequently shown to the Dermatological Society of London. The clinical appearance had not changed appreciably in the interval. She had now come up to Dr. Sequeira's clinic for treatment. A section of the skin was obtained by Dr. Little seven years ago, and the specimen exhibited at the meeting showed the characteristic appearances of the disease as described by Balzer, Darier and others. The elastic tissue seemed to form the bulk of the tumor; it was greatly increased in quantity and was swollen and broken up into fragments and granular debris which occupied the corium below the papillary zone.

The president of the society said he remembered that many years ago Sir Malcolm Morris asked him to go and see two sisters from Ireland, in whom the diagnosis of pseudoxanthoma elasticum of the neck was made. Their condition looked exactly like that in the present case.

*Herxheimer and Hell's*¹³ *Case*.—Herxheimer and Hell describe a rather exceptional case of pseudoxanthoma elasticum occurring in a boy 16 years old, who had always been in good health, who came for treatment of a weeping eczema, which healed in a few weeks. A skin lesion was noted on the face which had existed since birth, but which had caused no symptoms. None of the family showed similar lesions.

The lesions were symmetrically arranged on both cheeks, on both eyes, upward along the side of the eyes and downward to the corners of the mouth. The upper border was sharply defined; at the side and lower edge, the transition to normal skin was gradual. The lesions were made up of small trabeculae, with spaces not larger than a pinhead between them, forming a regular small network. The lesion had a duller appearance than the normal skin and was rough and uneven to the touch. Otherwise there was no alteration in the consistency. The elasticity of the skin appeared normal.

The patient was small but in good health and strong. A physical examination and urinary tests revealed nothing abnormal.

A piece of the lesion was excised from the left cheek, fixed in liquor formeldelydi and alcohol. Sections were mounted in paraffin. Microscopic examination showed the following:

With a hematoxylin-eosin stain the epidermis showed an irregular surface and was thinner than normal, with only 3 to 4 cell layers. The surface capillaries were slightly widened. In the connective tissue, there was some lymphocyte infiltration around the vessels. Where the atrophy of the epidermis and the rete was most marked, there were circumscribed lesions staining pale rose, usually round and almost entirely without nuclei. These lay under the epidermis, in the region of the pars papillaris, with the epidermis apparently arched over them.

With a cresol-violet stain the same morphology as in the foregoing was shown. The epidermis and connective tissue showed the normal violet shade.

12. Little and Sequeira: Case Presentation, Brit. J. Dermat. **22**:131, 1910; note by Calcott Fox—two sisters in Ireland had been seen by him.

13. Herxheimer and Hell: Eine Beitrag zur Kenntniss des Pseudoxanthoma elasticum, Arch. f. Dermat. u. Syph. **111**:761, 1912 (two histologic figures).

The circumscribed lesions noted with the hematoxylin-eosin stain showed sometimes a darker and sometimes a lighter shade, and were sharply marked off from the surrounding tissue. These small lesions never extended to the basal layer of the epidermis, as there was always a narrow unstained zone between. With the high power microscope, these lesions were seen to be made up of a thick, tangled maze of apparently regular fibers, some thin, some thicker, irregularly intertwined. Sometimes the mass was not so thick or so clearly defined, and the fibers were less intensely stained.

With carmin-lithium-carbonate and with the van Gieson stain, these lesions appeared very pale; with hematoxylin-eosin stain, steel blue; with Unna's universal stain, brown; with the Unna-Taenzer stain, reddish brown; with Unna's elacin stain, brownish red, single fibers in the vicinity, brownish blue. With these stains the single fibers were clearly visible, and the lesions were sharply distinguished from the surrounding tissue.

With Wiegert's stain, the elastic fibers of these lesions, staining a bluish-black, were clearly distinguished. In some places the single fibers were abnormally thickened and swollen. The transition from normal elastic fibers could also be seen.

The fourfold stain of Frenkel showed the epidermis yellow, the connective tissue dark green, and the pathologic lesions reddish brown. With a high power microscope the single elastic fibers were seen, with a few green connective tissue fibers among them, especially on the borders of the lesions.

Concerning the etiology of the condition, Herxheimer and Hell express the opinion that this is unknown.

*Kingbury and Heimann's*¹⁴ *Case*.—A girl, 21 years of age, born in England, who had been living in the United States for the past six months, had lesions which had been present on the sides of the neck for five years. They were rounded or oval, slightly elevated, buff colored patches about a half inch in width. Urinalysis two months ago showed 0.92 glucose. Two subsequent examinations were negative.

The microscopic examination showed that the epidermis was normal, as was the contour of the papillary body. The collagen was swollen at all levels, and there was a slight numerical increase of the fibroblasts. Vessels were not increased in number but were slightly dilated, without being engorged. Their endothelial lining was somewhat swollen, and outside a few vessels was a trifling infiltration consisting entirely of fibroblasts, arranged in one or two concentric rows. The most significant changes appeared in the elastic tissue, which was fragmented, curled back and formed in clumps of disrupted fibrils, or found isolated in broken strands. Some of the fibers stained blue with Unna's polychrome methylene blue dye. No plasma cells, giant or xanthoma cells were found.

*Mito's*¹⁵ *Case*.—About six years ago an otherwise healthy woman, 27 years old, without any subjective symptoms, noticed small, round, slightly raised hard spots with yellow to brown coloring on the neck, in the axillae and about the navel. Sometimes these small spots ran together. In between the skin seemed normal. In the middle cutis was a dark colored focus, which microscopically

14. Kingsbury and Heimann: Case for Diagnosis (Yellow Lesions on Neck), *J. Cutan. Dis.* **34**:377, 1916.

15. Mito: Ein Fall von Pseudoxanthoma elasticum, Japan. *Ztschr. f. Dermat. u. Urol.* **20**:No. 2, 1920.

Author	Year Reported	Case No.	Age	Sex	Nationality	Duration	Subjective Symptoms	Localization	Color	Clinical Picture	Site of Histologic Change	Histologic Picture	Complications	Remarks
Balzer.....	1884	1	49	M	French	Since childhood; was more marked	Mild itch in beginning	Neck, axillae, elbows, navel, less at inguinal and popliteal regions	Pale yellow	Flat xanthelasmatic plaques 1 sq. cm. to 1 sq. mm.; long axis with skin folds; forms small elevations	Hypertrophy of elastic tissue; fibers loosened, broken, knotty, wreath-like; often binding of destroyed and healthy fibers; little fat and few xanthelasmatic cells in modified skin	Formerly malaria; now pulmonary tuberculosis	At necropsy, same kind of spots found on endocardium and myocardium as on skin
Darier, also Chaffard, also Besnier, also Doyen, also Hellebrass and Lafitte	1896	2	42	M	French	16 years; for 7 years somewhat larger	Tender to touch	Symmetrical on neck, clavicular regions, axillae, elbow, abdomen, especially below navel, groin, under surface of penis, anal cleft and popliteal space; small lesions on upper lip, mucosa of lip and cheek and palpebral commissure	In beginning bluish, now yellow like cat's-paw-lait	Xanthoma-like spots elevated, 5 cm. broad and 10 cm. long; slightly uneven and made up of hemp to lentil sized spots; skin soft and pasty like moist velvet, slightly elastic; at periphery, small yellow or white plaques	Entire depth of cutis	Rounded off, not sharply limited lobes or coils showing laceration, swelling, disintegration of increased elastic tissue even to crumbling (elastoclasis, elastorrhexis); elastic tissue inclines toward basophilic; connective tissue almost normal; connective tissue cells increased at site of elastoclasis	Typhoid at 23; alcoholic gastritis; now fetid; now pulmonary tuberculosis	Small healthy strips present between epidermis and affection on mucosa of mouth; identity of yellow spots on palpebral commissures with the remainder not clearly evidenced
Bodin.....	1940	3	50	M	French	30 years; after some years increased	None	Symmetrical on lower abdomen, clavicular and axillary regions, inner surface of arms and genitocrural regions	Faded yellow	Round or oval pinhead to lentil sized, individual, grouped, or confluent papules forming plaques	Middle layer of cutis	Papillary bodies somewhat flattened; new perivascular infiltration; elastic tissue split, twisted, forming crumbling masses connected with healthy tissue; connective tissue bundles crowding one another; volume increased	Digestive disturbance; diarrhoea; uricæmia; negative for sugar; phthisis	Immunizable; multinuclear giant cells (Kölin cells) especially in periphery of masses about vessels
Von Tannenhain	1901	4	74	F	German	Anterior surface of upper arms, upper calves, about crests of ilium, less under chin and site of breasts	Opaque and yellowish	Irregular millet seed sized papules, some forming plaques; infiltration evident	Upper cutis	Flattened papillary body, roughly limited oval masses in them; swelling; separation into fibers; rolling together of elastic fibers; in part granular disintegration; connection of elastic cords with healthy tissue; connective tissue trabeculae greatly swollen and becoming homogenized	Arteriosclerosis; endocarditis; semileucæmia; pneumonia; intestinal hemorrhages	Calcification and formation of hyaline layer found at necropsy as secondary findings
Dühendorfer	1923	5	7	M	German	None	Left upper gluteal region unsymmetrical	Faint yellow	Palm sized flat elongated stripes and spots 1 by $\frac{1}{4}$ to $\frac{1}{2}$ cm., sharply circumscribed and slightly elevated; meshy network indented; minimal resistance	Middle and deep layer of cutis	Irregularly swollen and confused elastic bundles and broad bands; between them only collagen tissue; transition into healthy thrombi; collection of cells about vessels and follicles	Mild psoriasis	Numerous mast cells; not accepted by an as case of pseudo-xanthoma elasticum

TABLE 1.—CASE RÉSUMÉ IN CHRONOLOGICAL ORDER—(Continued)

Author	Year Reported	Case No.	Age	Sex	Nationality	Duration	Subjective Symptoms	Localization	Color	Clinical Picture	Site of Histologic Change	Histologic Picture	Complications	Remarks
Wertheimer.....	1904	6	26	F	Irish	12 years; very little increase	Mild itching	Neck anterior axillary folds and elbows	Ivory color with light bluish tone	2 to 3 mm. round, smooth soft papules, many running together to an irregular nest; little elasticity of skin	Middle and deep layers of cutis	Swelling and orderly mass of elastic bundles, disintegration of same (as if septums had formed) partly basophilic reaction; collagen trabeculae thick and swollen with proliferation of nuclei; marked increase of endothelial lining of small blood vessels	Chronic gas-tritis; freckles on face; chloasma	2 of 5 brothers and sisters have same affection since 13 years old; same localization; incised wound led to keloid; innumerable mast cells in lesion
Gutmann.....	1905	7	23	F	German	Earliest childhood	Entire circumference of neck	Whitish to ivory color	Plaques, single or in rows, confluent into a narrow nest; firmer than surrounding skin	Middle and deep layer of cutis	Epidermis thinned in places; papillary bodies flattened; transition into healthy tissue from clumpy masses of swollen, knobby, distended, partly fragmented or granulated broken-up elastic bundles demonstrated; elastic not clearly demonstrated; collagen tissue in lesion decreased	Chancroid between eyes; freckles on face, arms and hands	
Dohl.....	1907	8	74	F	German	20 years	None	Symmetrical; forehead, eyelid, cheek, upper lip and chin	Straw yellow to lowish brown	Pinhead to lentil sized flat, smooth, sharply margined elevations, somewhat harder than normal skin, either isolated or fused into network	Middle and deep layer of cutis	Coil and clump formation of elastic bundles, which are swollen and ligament-like; elastic reaction negative; connective tissue trabeculae somewhat coarser than normal; otherwise connective tissue unchanged	Chorosis; freckles; macular syphilid	1 brother and 1 sister have had same disease since early childhood; isolated giant cells present
Little.....	1908	9	56	F	English	20 years	None	Whole neck, flexures of elbows	Buff color	Meshlike patch of buff-colored infiltrations, lumpiness in places, in others linear and hardly raised from surface	No biopsy reported	Epidermis somewhat and papillae entirely atrophied; round or oval groups of enlarged basophilic reacting elastic tissue bundles shown between which collagen fibers are decreased; increase of connective tissue indicates size of lesion; homogeneous compact collagen mass with basophilic reaction (Kollazin); pigment increased	Pterygium	Mast cells present; (this case not always accepted, but Herxheimer and Hell include it as an example of the disease)
Bosellini.....	1909	10	45	F	Italian	6 to 7 years on forehead; 3 to 4 years on hands	None	Symmetrical; forehead, and contiguous portions of root of nose and cheek regions, flexor surface of thumb and index fingers (as bands 1 cm. broad)	Slate brown color	Millet seed to hemp seed sized hemispherical, smooth, skinny elevations, arranged like herpetic lesions, separated from each other by regular grooves; on hand verruca-nevoid in form	Middle cutis	Epidermis somewhat and papillae entirely atrophied; round or oval groups of enlarged basophilic reacting elastic tissue bundles shown between which collagen fibers are decreased; increase of connective tissue indicates size of lesion; homogeneous compact collagen mass with basophilic reaction (Kollazin); pigment increased		

Pinkus.....	1910	11	53? 47?	F	German	Neck, axillae, elbows, navel region, inguinal folds, upper leg, sparse at knees	Yellow- ish	Arranged in stripes, half circles and el- lips are pinhead to lentil size papules be- tween which skin is slightly depressed and shiny with light bluish tint; folds of axillae and groins hang pendulous	Deep cutis	Lesions consist of crumbly, curly, inter- locking elastic bundles which look like thick decayed partly dis- solved elastic bundles, or as if only part of the elastic cortex was left	Tertiary syphilis	Scars on neck probably from anæ; lost weight last year; skin of axillae thick as leather and hangs in folds
Little and Sequeira	1910	12	19	F	English	Cutis under papillary bodies	Elastic tissue seemed to form bulk of tumor; greatly increased in quantity, swollen and broken up into frag- ments or granular debris	No change since seen seven years pre- viously
Herxheimer and Hell	1912	13	16	M	German	None	Earliest childhood	Symmetrical on cheeks	Normal to light pale	Seemingly orderly tel- lis work of fine trabe- culae; between are pinhead sized clear fields	Papil- lary body	Sharply circumscribed fool made up of thick maze of thickened, apparently orderly, elastic bundles with only occasional transi- tion into normal	Eczema of head
Kingsbury and Hel- mann	1916	14	21	F	English	5 years	Sides of neck.....	Buff colored	Rounded or oval slightly elevated, about 1/2 inch in width	All levels	Collagen swollen; slight increase of fibro- blasts; elastic tissue fragmented, curled back and formed in clumps of disrupted fibrils or isolated in broken strands; no plasma, giant or xanthoma cells	One urine exam- ination; 0.92 glucose; two other examina- tions negative
Mito.....	1920	15	27	F	Japan- ese	None	6 years	Neck, axillae and na- vel region	Yellow to brown	Pinhead to linseed size round slightly raised hard spots with smooth yellow to brownish coloring which sometimes ran together; in between skin normal	Middle cutis	Thick, bandlike, disor- derly, broken, clumpy or crumbled bundles; about the neighborhood of lesion, one could dis- tinguish transition of bundles into elastic; xanthoma cells not found	Healthy
Our case.....	1921	16	39	F	Ameri- can	None	35 years	Symmetrical; neck, axillae, flexor surface of arms and fore- arms	Fresh butter yellow	Yellowish small papu- lar elements, individ- ual and confluent, or massed into plaques; grossly thickened skin where lesions exist; exaggeration of normal creases and reduplication of normal folds	Lower and middle derma	Clumps of swollen and degenerated elastic fibers with basic degen- eration of collagen fibers in lesions; little change in pars papil- laris of derma; sweat and sebaceous glands and hair follicles not involved; no giant or xanthoma cells	Enlarged mediastinal glands	One sister had similar condi- tion; died at age of 34 of tuberculosis

showed many thick bandlike disorderly broken clumpy or crumbled bundles. About the neighborhood of these foci, one could distinguish the transition of these bundles into normal elastica. Xanthoma cells were not found.

ETIOLOGY

Age.—In the fourteen reported cases in which the ages of the patients are noted, they have varied from 7 years, the youngest, to 74 years, the oldest.

Sex.—There has been a preponderance of female cases. Of the 20 cases (those reported and those only mentioned) in which the sex is given, six have been males and fourteen have been females.

Nationality.—There have been six cases reported in full from Germany, and in addition, two other patients have been mentioned who were German. One case in a native of Ireland has been reported in full, and mention has been made in the literature of four others. Three patients were French, three English, and one each were from Italy and Japan. Our case was that of an American woman of German parentage.

Associated Diseases.—Three of the reported cases were in patients with pulmonary tuberculosis. Our patient presented findings which led to the belief that she may have had tuberculosis, which at this time is inactive. The sister of our patient, who had the same disease, died of pulmonary tuberculosis. One patient is reported as showing a secondary macular syphilid, and another patient had a concomitant tertiary syphilid. Gastritis is mentioned three times as an associated disease. Two of the patients had freckles, and one had superficial epitheliomas. A list of the other diseases which were found includes: pterygium, arteriosclerosis, myocarditis, pneumonia, psoriasis and eczema. Except for the tuberculosis, no claim for causal or distant relation has been advanced. One patient, in addition to ours showed a slight transient glycosuria.

Familial Characters.—In two of the reported cases, two other members of the family had the same condition, which became apparent when the same age was reached. Colcott Fox, in the discussion of Little's case, mentioned that he had once been called to see two sisters who were suffering with the affection. A sister of our patient had the same character of eruption. In both sisters it appeared when they were each 4 years old.

Age of Onset.—The age of the onset is given as since earliest childhood or since childhood in four cases. In eight others, the age of the onset is given as: 10, 16, 18, 20, 38, 46 and 54. In our patient and in her sister the onset was at 4 years of age.

Duration.—In the cases reported the duration has been given as four, five, six, seven, twelve, sixteen, twenty, and in one case thirty years. Our patient had the disease thirty-five years. Her sister had the affection for thirty years before she died.

Subjective Symptoms.—In ten reports, subjective symptoms have been mentioned. In eight of these, the absence of subjective symptoms is commented on and in two mild itching is noted.

Color.—In the cases in which color has been reported, the following range has been covered: normal to light pale, whitish to ivory, ivory color with light bluish tinge, yellow to opaque, pale yellow, faint yellow, yellowish, sulphur yellow, yellow like, café au lait, straw yellow, to yellowish brown, yellow to brown and slate brown to lead color. Fresh butter yellow fits the individual lesions of our case and a tawny yellow the flat lesions in the cubital spaces.

TABLE 2.—LOCATION OF PSEUDOXANTHOMA ELASTICUM

Face.....	3	Ilium.....	1
Neck.....	9	Inguinal regions.....	4
Under chin.....	2	Gluteal region.....	1
Clavicular regions.....	2	Penis.....	1
Axillae.....	7	Anus.....	1
Elbows.....	5	Upper leg.....	1
Arms.....	2	Popliteal spaces.....	2
Fingers.....	1	Upper calf.....	1
Breast.....	1	Not mentioned.....	1
Navel.....	6		

SUMMARY

We have clinically identified a case of pseudoxanthoma elasticum which is one of the rarest dermatoses accepted as an entity. Our case was in a young woman, 39 years of age, who had had the affection since she was 4 years old. Of her circle of relatives, one sister had had a similar condition since she was about 4 years old, and as has been reported for some of the cases, her death was attributed to tuberculosis. Our patient had had a lymph node incised when eighteen months old, and at the present time shows enlarged mediastinal glands on roentgen-ray examination. This is little evidence on which to base a diagnosis of accompanying tuberculosis. The clinical picture in our patient fits that of the published cases. Individual papular butter yellow lesions, with a tendency to confluence, as evidenced by the groups of twos and threes, and the plaque lesions of which there are two varieties, the raised and the flat, have been described for this disease. The folds and exaggerated creases are also part of the accepted clinical manifestations.

Histologically the clinical diagnosis was confirmed. The lower and middle derma showed clumps of swollen and degenerated elastic

fibers with basic degeneration of the collagen fibers in the lesions. This change in the collagen has not been previously thought to be an important change, but in our case it has seemed that the collagen changes are significant. There was little change in the epidermis and the pars papillaris of the derma. Sweat and sebaceous glands and hair follicles were not involved. No giant cells were present and no xanthoma cells.

CONCLUSIONS

1. Pseudoxanthoma elasticum possesses clinical, morphologic and histologic characters that are unlike those of any other known dermatosis. It is, therefore, an entity.

2. The essential clinical features are: yellowish, small papular elements, individual and confluent, or massed into plaques; grossly thickened skin where the lesions exist, although this may not be constant; exaggeration of the normal creases, and reduplication of the normal folds. The neck and the axillae are apparently the sites of predilection.

3. The essential histologic features are: clumps of swollen and degenerated elastic fibers with basic degeneration of the collagen fibers in the lower and middle derma. There is little change in the epidermis and the pars papillaris of the derma. The sweat and sebaceous glands and the hair follicles are not involved. There were no giant or xanthoma cells, although Bodin has found the former.

4. The etiology is unknown. It has been considered a nevus, a form of tumor, and from an association with tuberculosis, as dependent on that disease for its causation. It has been thought to be an idiopathic degeneration, but that does not make the etiology any clearer. It may prove to be dependent on a degeneration of the nerve elements in the situations where the disease exists.

5. One can demonstrate all the characters necessary for a diagnosis. The case clinically identified by us, studied histologically, and here reported, resembles in nearly every respect the classical description of pseudoxanthoma elasticum.

We desire to thank Dr. H. H. Whitehouse for allowing us to report this case. We wish also to express our appreciation of Dr. Elizabeth Finch's¹⁶ kindness in helping in the study and interpretation of the histologic material.

ADDENDA

Since the report given in the foregoing has gone to press, another instance of pseudoxanthoma elasticum has been seen at the New York

16. Dr. Finch died June 21, 1921.

Skin and Cancer Hospital in the service of Dr. A. Schuyler Clark, to whom we are indebted for the privilege of reporting it.

Mrs. M., an Italian woman, 42 years old, came to the dispensary for treatment for psoriasis. The added condition of pseudoxanthoma elasticum was noted during the examination. The patient said that she had first noticed the lesions of pseudoxanthoma when she was about 12 years old. No other member of the family had a similiar disease. The family history was negative for tuberculosis and diabetes mellitus. The patient refused to permit a biopsy, or venipuncture.

The lesions were present in the same regions as on the patient of our more detailed report. Inguinal lesions were also present. The lesions on the neck were practically identical with those of the earlier case. The skin did not hang in folds, and the discrete lesions were more widely distributed, being found over the shoulders. In the axillae and anterior cubital flexures the lesions were similar to those in the first case. No lesions were present on the face.

The patient made only one visit.

STAINING OF SPIROCHAETA PALLIDA BY THE FONTANA-TRIBONDEAU METHOD

ELIMINATION OF HEAT

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Our chief purpose in beginning our investigation was to discover a quick and reliable method, which could be employed by any one familiar with microscopic work, to demonstrate *Spirochaeta pallida* in the transudate of a chancre as easily as the tubercle bacillus is demonstrated in the sputum.

Nowadays, as we gain a better knowledge of the invasion of the tissues by the spirochete, when a patient with a so-called second syphilitic incubation is considered to have a possible case of the dreaded nervous involvement, it is convenient for the specialist to have a simple, reliable method to diagnose and to differentiate the chancre. With this in mind we searched for a staining method which should fill these requirements.

Our advocacy of this method does not mean that we consider it superior to the dark-field method, since both methods have their own advantages, but not all laboratories are equipped for dark-field demonstrations.

DIFFERENT METHODS

Giemsa's method, based on the capacity of protozoa to stain with azur or azur derivatives and Levaditi's silver nitrate method are the technics from which many others originated. Among these, the one that seemed best to us on account of its quickness and reliability was Fontana-Tribondeau's.

For this method the following things are needed:

1. A substance to dissolve the hemoglobin in the blood serum from the chancre.
2. Deep fixation.
3. A mordant.
4. Impregnation with silver nitrate without any reducing mixture.

The spirochetes assume a light purple to dark brown color, according to the handling of the technic. This procedure has in its favor the fact that it is quick and reliable; it is possible to stain a specimen in five minutes, and the identification does not take any longer than with any other preparation. As the spirochetes are very delicate organisms it

might be that roughness in the technic through changing their spiral form might be responsible for the many differences often detected in their appearance. This turned our attention to the fact that heat plays a very important part in Tribondeau's technic. In fact, fixation is done by pouring and burning alcohol over the slide. The application of the mordant requires exposure to the flame until it smokes. When the stain is applied it must be kept steaming during a period of thirty seconds.

In our efforts to do away with heat, we tried, first, fixation with burning alcohol. The slides were fixed in the usual way but without using alcohol in the cover glass. Cover glasses cannot stand the heat of the flame without breaking, and as we intended to use them to avoid any silver nitrate stains, as happens with slides, this was another difficulty.

Specimens both with and without alcohol show the spirochetes perfectly. If we keep in mind the fact that the dechemoglobinizng solution serves for fixing just as well, we will realize that a deep fixation is not necessary. Naturally the best proof is found in the result obtained with the controls. As soon as we stopped the use of alcohol, we began to use a cold tannin solution. We made repeated applications during three, four, five and seven minutes, finding that the silver nitrate showed only slightly the desired metallic shade, as there appeared in weak tints red cells, white cells, spirochetes, and other elements of the transudate. We increased the time to ten minutes and we then had satisfactory preparations.

TECHNIC

The preparation of the silver solution includes three steps:

1. Formation of the precipitate.
2. The solution of it with an excess of reagent.
3. Formation of the new precipitate, adding silver nitrate until it turns an opalescent shade.

If more silver solution is poured in, this shade changes to dark brown. If we let it stand, in about an hour there will be at the bottom of the flask a flaky black precipitate and a colorless supernatant fluid; if the precipitate is disturbed it will not lose its flaky character or its staining qualities, but it will have the disadvantage of settling on the slide preparation. After twenty-four hours, it behaves as reported.

In order to find out whether it was essential to heat the silver nitrate solution to stain the spirochetes, controls were made in a cold solution during one, three, and five minutes. Those exposed to the action of the stain for three minutes seemed satisfactory, both the organisms and cell elements appearing well stained, and equaling those submitted to

heat. However, it is fair to add that the reagent was used with an amount of silver nitrate sufficient to form a dark brown solution.

We have stated before that this dark brown color appeared twice, and in order to facilitate its appearance we decided to use a definite quantity of 5 per cent. silver nitrate, and another definite quantity of ammonia, either diluted or undiluted, as this would make the technic more accurate. We took 5 c.c. of silver nitrate and a drop of 50 per cent. ammonia. With this proportion we obtained at once the desired shade. But it seemed as if the diluted ammonia lost its strength, and we decided to use it pure, securing then better results. After studying the action of heat on the morphology of *Spirochaeta pallida*, we have come to the conclusion that the best results are obtained when the reagents are applied cold.

The reagents employed are: glacial acetic acid, 1 c.c., formaldehyd, 2 c.c. and distilled water, 100 c.c.; tannin, 5 per cent., 100 c.c.; silver nitrate, 100 c.c.; ammonia, pure, 10 c.c.

The reagents are used in the following order: Ruge's solution, for several immersions; distilled water; tannin heated until it smokes, and then employed thirty seconds; distilled water; ammoniated silver nitrate precipitate, cold, employed two seconds and in distilled water. Mount in glycerin, using paraffin margins.

CONCLUSIONS¹

1. Burnt alcohol fixation is not necessary, but is, on the contrary, rather harmful to the morphology of *Spirochaeta pallida*.
2. Ruge's solution is sufficient for fixation and dehemoglobinization.
3. This solution can, however, be substituted by H₂O₂, one-third in water and 1 c. c. formaldehyd, making a volume of 100 c. c.
4. Heat is not essential in order that the tannin may act as a mordant.
5. Fontana's solution may act without heating.
6. The best way to use the method consists in heating tannin until it steams, and applying silver nitrate for one or two minutes.
7. The most typical forms of spirochete are seen when the method is applied cold.

1. The staining of *Leptospira icteroides*, both hot and cold, leads us to the same conclusions.

A COMPARISON OF INGREDIENTS OF RINGWORM CULTURE MEDIUMS

WITH SPECIAL REFERENCE TO AMERICAN AND FRENCH CRUDE MALTOSE *

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AND

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PHILADELPHIA

It will be unnecessary to explain the need for the work above indicated to any one who has attempted the culture, particularly the identification of the ringworm fungi. For the sake of others, let it be said, first, that the proposition is very different from the cultivation of the bacteria, and that the difficulties are not along microscopic lines, but preeminently from the gross morphologic standpoint. Yet more precisely, we are not concerned so much with the matter of luxuriance of growth, for at present our fungi grow easily enough. Rather are we trying to coax out differential characteristics. It is with the latter phase that this paper has to deal; but before proceeding to our experimental work some preliminary considerations must be offered to make the work understandable.

The problems before us can best be comprehended by keeping in mind throughout that the molds are plants. Much higher than the bacteria, they consist in most cases not alone of the more vegetative structures, such as the mycelia, which may be compared to stems of plants, but also of reproductive bodies which may be compared to the flowers and fruit. Keeping this in mind, it will at once be appreciated that differences in the medium on which the mold is planted must be expected to produce some order of change in gross morphology, just as variation in the composition of the soil would make a difference in the appearance of a tomato plant. That is, depending on the amount of moisture available, the amount of nutritive substances, such as phosphorus, nitrogen, inorganic salts, etc., we may get anything from a yellow, scrawny, fruitless plant a foot or so high, up to the rank, deep green, fruitful growth with which everybody is familiar. While indulging in this comparison, let us recall that the appearance of plants will be different, too, at different stages of their growth.

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*Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

All of these considerations hold good for the molds, and as a result we find that their appearance will vary with age, the composition of the medium, its acidity, its moistness, and even the thickness of the stratum on which it is growing. For purposes of identification, therefore, it is necessary that, as a rule, the age of the colony be known (or better the course of its growth be followed from the time it is planted until full maturity), the composition of the medium be precise and the thickness of the stratum be uniform.

MORPHOLOGIC VARIATION

One can better understand why bacteria show less morphologic variation than the molds when one recalls their finer, microscopic



Fig. 1.—Culture Series 1. *Trichophyton effractum*, colonies nine weeks old. First six tubes "all French" ingredients except Tubes 2 and 6 which have American agar; Tube 7, "all French" except for Difco peptone; tubes on bottom row, all American ingredients: first tube, Pfanstiehl maltose; second, Difco; third, Mellin's; fourth, Eflorose; fifth, Dolbey; sixth, Borchardt's; seventh, Mead's. No acid adjustment. Color and texture were the same on all. The cracks are characteristic on all "all French" tubes, and suggestive on several on the bottom row.

appearance. These more primitive plants consist of cells more dissociated; and the cohesion of the cells, the direction of growth, extension, etc., is therefore more limited than in the case of molds. The latter, having mycelia, can creep outward or upward or interlace with one another, just as vines creep over a rock, or, by becoming more or less compacted and felted together, can lead to a looser or more compact macroscopic appearance, depending on the propensities of the

species. It is this variable, close felting of mycelia which is responsible for the various downy or furry or hairy qualities of different species of mold cultures. Depending on the robustness of the mycelia and the question whether they are entwined into wisps or not, the surface of the colony will appear from delicately downy to coarsely furry.

A further surface feature of the molds is the presence in some species of a powder. An analogous phenomenon does not appear in bacteria because this powder is referable to microscopic-size fructifications of one or another sort (conidia, fuseaux, etc.) which are not produced by bacteria.

The result of all these considerations is that, by way of contrast, a colony of staphylococci, if grown on continually moist agar as we grow our molds, will maintain about the same moist, smooth, glistening



Fig. 2.—Culture Series 1. *Microsporon fulvum*; colonies four weeks old. Tube at left “all French”; at right, Mead’s. No acid adjustment. To all intents and purposes they are identical as mycology goes. Illustrates adequacy of several maltoses for this species.

surface over a period of many days or several weeks, whereas a mold will appear materially different. Taking *Microsporon lanosum*, for instance: In the first day or two we see but a few tufts of white down; in the course of a week a coffee-brown powder begins to appear in the center, and a little later this becomes rather extensive. Gradually, during the course of a few weeks more, the powder is overgrown and covered by the down, until by the end of six or eight weeks the colony consists solely of the latter, and has an appearance indistinguishable, in this late stage, from many other fungi.

To go a little further: Suppose the composition of the medium on which our bacterial and fungus colonies were growing were altered in some respect. We should find that in the case of the bacterial growth

a rather radical change would be necessary in order to change the character of the colony even moderately, such as a variation of sugars, or even the transference to a very different medium, such as potato, gelatin, etc. But with the fungi such changes would work most striking changes in morphology, and it is this sensitiveness on the part of pathogenic fungi to comparatively trivial variations in the medium that has made this study necessary. In essence, it is the higher degree of specialization of these fungi, compared to bacteria, that enables them to take on such different appearances—depending on the nutritional conditions which happen to be at hand.

LACK OF SATISFACTORY CLASSIFICATION

We believe that it is this inconstancy of morphology which has been the big stumbling block to a more general, certainly a more continued, study of the molds. But this is not all. A second obstacle consists in the fact that at present there are no satisfactory classifications of the



Fig. 3.—Culture Series 1. *Epidermophyton inguinale*; colony four weeks old. Tube 1, "all French" ingredients except the agar; Tube 2, "all French"; Tube 3, Mead's; Tube 4, Eflorose. No acid adjustment. Allowing for the "individual variation" of mold colonies, as far as appearance goes all four of these might have been planted on the same medium. Illustrates comparative adequacy of several maltoses for this species.

fungi from the systematic standpoint. Sabouraud's is a clinical one which depends on a foreknowledge of the source of the material, and only covers a limited number of species as compared to the whole broad general subject of mycology. What Sabouraud has done he has done well; but one has only to examine the list of names applied to genera (*Microsporon*, *Trichophyton*, *Epidermophyton*, *Achorion*) to recognize the futility of attempting to classify nonpathogenic fungi in relation to those from the systematic, botanical standpoint.

Castellani,¹ on the other hand, has given us a tentative working classification along these very lines, i. e., an arrangement into classes,

1. Castellani, A.: Milroy Lectures, J. Trop. M. **23**:101 (May 1) 1920; cont. **23**:117 (May 15) 1920; cont. **23**:133 (June 1) 1920.

orders, families, genera, etc., depending on the morphology of the organism. This is the rational classification, comparable and consistent with the classifications applied in biologic systems. The unfortunate feature of Castellani's classification is that he does not go far enough in that he fails to analyze Sabouraud's genera and to distribute the very differently appearing species under the proper genera. Examples are the achorions. The microscopic characters of *A. schönleinii* are very different from those of *A. gallinae* and *A. quinckeanum*. We might also cite *Trichophyton faviforme*. In short, what we need today is a revision of the classification of the fungi from the morphologic



Fig. 4.—Culture Series 1. *Epidermophyton inguinale*; colony nine weeks old. Tubes 1 to 6 “all French” ingredients: Tube 7, “all French” except for Difco peptone. Bottom row: all American ingredients: first tube, Pfanstiehl maltose; second, Difco; third, Mellin's; fourth, Eflorose; fifth, Dolbey; sixth, Borchardt's; seventh, Mead's. No acid adjustment. The Difco peptone and American maltose are a little remiss in not developing the peripheral fringe at this late date, but sufficient criteria still remain for certain identification. Illustrates comparative adequacy of several maltoses for this species.

(essentially microscopic) standpoint. With this at hand, supplemented preferably by an encyclopedic textbook, with full illustrations of type fructifications and other “organes,” we should not experience a feeling of despair as we now do when we isolate an organism which does not compare with those illustrated in Sabouraud's or Castellani's books.

THE RESTRICTED FIELD OF MYCOLOGY

In the third place, mycology has a very restricted field. Its practical application lies in greatest part at present in the subject of ringworm: and, as this is not a matter of life and death ordinarily, there is not the zest to the subject that there is to that of bacteriology and animal parasitology. It is not as profitable a field as those, certainly not in proportion to the difficulties to be overcome.

We believe these factors are the three major lions in the way of progress in mycology. Of them the second, classification, cannot logically and seriously be attacked until the first, morphology, has been disposed of and made available for use in constructing a classification. The third will take care of itself, and the field broaden as it is cultivated.



Fig. 5. Culture Series 1. *Microsporon equinum*. Colonies four weeks old. Tube 1, "all French" except the agar; Tube 2, "all French" except for Difco peptone; Tube 3, Difco maltose; Tube 4, Pfanstiehl; Tube 5, Mellin's. No acid adjustment. Striking contrast between the C. P. maltose (Tube 3) and the remaining four impure ones.

It would indeed be an achievement for such a subject as pulmonary sporotrichosis or systemic blastomycosis to be clarified by a dermatologist.

It is evident that all this is no one or two man task. We outline it rather to orient the general physician mycologically, and to explain the reason for our work here reported. This at present concerns the subject of culture mediums, a phase which is basic to, and indispensable for, any progress in mycology.

CULTURE MEDIUMS

The maltose ingredient has been every one's main concern so far. It is used in mediums today because the earliest workers began with it.

and because Sabouraud insisted so strongly on its use for bringing out differential characteristics. Bodin,² for instance, used beerwort. Colcott Fox³ and Sabouraud,⁴ who followed him, used a solidified refinement of the same substance in the form of a very crude maltose. Fox and Blaxall's experience with mediums reads very much like what we shall say later, except that they ascribed the high acidity to the maltose rather than to the peptone. They, too, finally had to resort to imported French ingredients.

White⁵ stood rather alone in finding that other maltoses (Lehn and Fink, and Grüblers) were equivalent to the crude French (Chanut).

The Maltose Situation in America.—As far as we can learn at present, few men have attempted the culture of ringworm fungi in America and at the same time seriously attempted to obtain the same morphologic characters that Sabouraud did. These men imported the French ingre-



Fig. 6.—Culture Series 3. *Microsporon equinum*; colonies ten days old. Tubes 1 and 2, "all French" control. Remaining seven on American peptone, with acidity adjusted to + 1.8 with "hydrochloric acid albuminate." Maltose as follows: Tube 3, Mead's; Tube 4, Borchardt's; tube 5, Mellin's; Tube 6, Pfianstiehl; Tube 7, Maltine; Tube 8, Difco; Tube 9, Dolbey. Obvious disagreements photographically with control except Tubes 3 and 6. The latter were too highly heaped up, and lacked the smaller secondary furrows. These differences increased as the colonies aged.

dients, and were therefore reasonably sure of comparable pictures. No doubt others, like ourselves, have attempted such work and obtained only passable results. Our experience is that some of Sabouraud's fungi give sufficiently characteristic growths for identification on mediums made from ordinary American trade ingredients. *E. inguinale* and *A. schönleinii* are examples, but others which do not grow typically

2. Bodin, E.: Les champignons parasites de l'homme, Paris, Masson et Cie. 1902, p. 107.

3. Fox, Colcott, and Blaxall: Brit. J. Dermat. 1896, pp. 242, 291, 337, 377.

4. Sabouraud: Les teignes, Paris, Masson et Cie, 1902.

5. White, C. J.: J. Cutan. Dis. **17**:1 (Jan.) 1899.

are the very important *M. audouini* and *M. lanosum*; and the gross appearance for these two is very important, because with several species closely related to them the microscopic appearance is identical, and gross appearances are therefore indispensable in order to distinguish them differentially. Compare *M. audouini* and *M. velveticum*, on the one hand, and the whole group of animal microsporons on the other.



Fig. 7.—Culture Series 3. *Microsporon equinum*; colonies ten days old. Adjusted to + 18 with "hydrochloric acid albuminate." Tubes 1 and 2, "all French" control; Tube 3, "all French" except for Difco peptone; Tube 4, R. A. L. maltose. The third colony is moist, and the fourth not hairy enough as compared to the two controls.



Fig. 8.—Culture Series 3. *Microsporon lanosum*; colonies ten days old. Tube 1, "all French" control. Remainder with Difco peptone, medium adjusted to + 1.8 with "hydrochloric acid albuminate" and containing American maltoses as follows: Tube 2, Mead's; Tube 3, Borchardt's; Tube 4, Mellin's; Tube 5, Pfanstiehl; Tube 6, Maltine; Tube 7, Difco; Tube 8, Dolbey. The differences became more marked as the colonies grew older.

Now, the problem would be much simplified if a supply of all the French ingredients were at all times easily obtainable; but this is not the case. While we have been able to import all the other substances, we have not yet succeeded in obtaining any of the French crude

maltose. Others have had very much the same experience. Mr. Hodges, from whom we obtained our supply, had succeeded in getting some through a personal friend who was himself on the ground in Paris. And now that Sabouraud⁶ writes us that there is no more crude maltose available, a fortunate departure has been precipitated from what was from the first an unsatisfactory medium for culture.

General Considerations of Sabouraud's Proof Medium.—This medium consists of:

Maltose (Chanut).....	40 gm.
Peptone (Chassaing).....	10 gm.
Agar	18 gm.
Water	1,000 c.c.

The maltose must be crude; the chemically pure will not do. Sabouraud's material is indeed crude, coming in fractured lumps about the color of sweet chocolate. The peptone is made by Chassaing, and we early found that it was the factor responsible for the rather high



Fig. 9.—Culture Series 3. *Microsporon equinum*: colonies ten days old; illustrating synthetic mixtures and inadequacy of dextrin combinations tried. Tubes 1 and 2, "all French" controls; Tube 3, dextrin 100 per cent. (of the whole sugar content) Difco maltose none; Tube 4, dextrin 90 per cent.—maltose 10 per cent.; Tube 5, dextrin 50 per cent.—maltose 50 per cent.; Tube 6, dextrin 10 per cent.—maltose 90 per cent. The last colony was really not as good as it looks photographically. It was too highly heaped up in the center, and not coarsely hairy enough.

acidity of the French medium as compared with the American (+1.8 against +1.2). When one recalls how the composition of different peptones varies, and that the maltose is perforce crude, one must realize beforehand that an attempt to imitate them will be only a

⁶ Sabouraud writes, May 12, 1921, that "ne trouve plus en ce moment" and "nous ne pouvons plus nous procurer de maltose Chanut." It appears that the history of the house of Chanut had been a checkered one. As far back as 1896 Colcott Fox and Blaxall (Footnote 3) stated that Sabouraud had told them that the factory was closed. In 1902 Bodin found that crude maltose was not procurable commercially (Footnote 2) "Ne se trouve plus dans le commerce." In spite of all this, small lots at least have within the last few years been filtering into America, and appear to be the genuine article.

hope for good fortune. Both are prepared by biologic methods, i. e., by the use of enzymes. Furthermore, the "impurities" in maltose consist not alone of such carbohydrates as dextrin and glucose, resulting from the incomplete enzymic action, but also certain nitrogenous substances. All of these will vary with the method of preparation of the specimen of crude maltose and are in themselves important substances in the nutrition of the fungus which is to be cultured. Therefore, the combination of these variables—peptone, maltose, impurities—appears

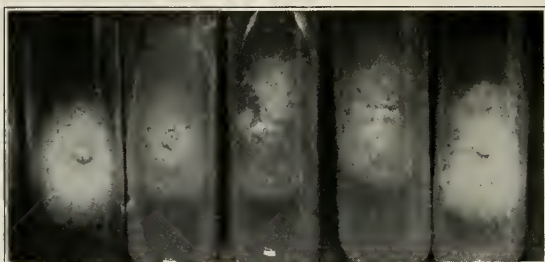


Fig. 10.—Culture Series 3. *Microsporon lanosum*; colonies ten days old. Same test and ingredients as in Figure 9, except that only one control is shown at the left. In both Figures 9 and 10 the last tubes show that it is the maltose that is almost "saving the dextrin's face," but falling short.

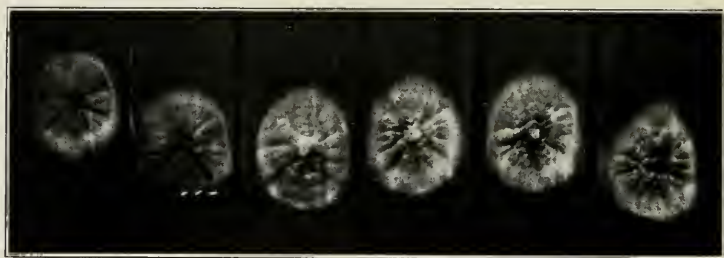


Fig. 11.—Culture Series 3. *Microsporon equinum*; colonies ten days old. Tubes 1 and 2, "all French" controls. Remaining four contain varying proportions of glucose and maltose; Tube 3, glucose 100 per cent. (of the whole carbohydrate content)—maltose none; tube 4, glucose 90 per cent.—Difco maltose 10 per cent.; Tube 5, glucose 50 per cent.—maltose 50 per cent.; Tube 6, glucose 10 per cent.—maltose 90 per cent. Whereas in the illustration all of the latter four appear very similar, yet there are characters (color, moistness, etc.) not brought out photographically which make the last combination the one of choice.

insurmountable. However, the final determination could only be made by trial.

AUTHORS' STUDIES

We have conducted four series of tests. In all, the tubes were run in duplicate, i. e., sowings were made on two tubes instead of one of

each of the many combinations. This was done to guard against interruption of the series by the occasional contaminations, the occasional unexplainable failure to "take," and the certain degree of individual variation that always obtains in ringworm colonies. Purity of our culture has always been kept in mind and controlled from time to time. In each series, a control was run on mediums made from imported "all French" ingredients, and the growth which developed on this (in duplicate as in all other tubes) was used as a standard. The general plan was to make various combinations of reactions and ingredients in mediums to see whether the growths developing on them would tally with the "all French." We have used nine different organisms, compounded about 300 combinations of maltoses, acidities,

TABLE 1.—VARIOUS BRANDS OF MALTOSE USED IN THE AUTHORS' TESTS *

	Maltose by Benedict	Barfoed†	Moisture	Achroo- dextrin
Difco Stiehl.....	100	Negative	0.0%
Pfanstehl	83	Strong	2.3%	14.7%
Dalbey	72	Strong	7.0%	21.0%
Borchardt	81	Moderate	2.5%	16.5%
Mead	55	Moderate	5.1%	39.9%
Mellin's	55	Weak	5.5%	39.5%
Maltine	66	Strong	30.0%	4.0%
Du Sabouraud ‡.....	104‡	Strong	10.7%	? §
R. A. L. ¶.....	65	Very Weak	19.0%	16.0%

* Approximate estimation by Dr. R. L. Stehle. Accurate figures are unobtainable for mixtures of carbohydrates on account of limitations of present chemical methods.

* There was no starch in any of the brands.

* Eflorose, a confectioners' syrup, used only in the first series of tests, was not analyzed.

† A positive Barfoed test represents the presence of dextrose. The maltose percentages therefore include dextrose, and the actual quantity of sugar present is smaller than indicated by the percentages, since the reducing power of dextrose exceeds that of maltose. The dextrin percentages are consequently somewhat higher than the figures given.

‡ This high figure is due to (1) the reducing "figure" of maltose being so low (as compared to glucose), and (2) the fact that glucose is so largely present in the mixture.

§ This figure not obtainable on account of the high figure for maltose. The dextrose figure is the difference between the maltose and moisture.

‡ Imported French. Furnished through the kindness of Mr. Robert L. Hodges, University of Alabama, and presumably the product of Chanut.

¶ Substitute crude maltose proposed by a French manufacturer.

peptones, etc., and as such were run in duplicate it has meant, counting the controls, that upward of 700 tubes have been studied in all.

Several of the specimens of maltose used (Table 1) will be recognized as proprietary infants' foods. As far as we could ascertain, only one chemically pure maltose is made in America (Difco).

Series 1.—In this series seven different known organisms were used as indicators, four of which were sent to us by Prof. Sabouraud and the remainder isolated in our laboratory. The following organisms were used: *M. lanosum*, *M. equinum*, *E. inguinale*, *T. cfractum*, *T. plicatile*, *T. radiolatum* and *T. gypsum* (Sabouraud).

We used ten different American sugars, filtered through both cotton and French and American filter papers, and with French and American agar. The stoppers of some tubes were paraffined or covered with lead foil to exclude air, and others were not. All tubes were kept in

semidarkness at room temperature. We found that the method of filtering had no effect on the cultures, that the same appearance obtained on American as on French agar, and that paraffining had no effect on the growth characteristics until after the lapse of the several weeks during which observations are of use in identifying these cultures. After that time the medium dried out naturally more rapidly than did the tubes stoppered with paraffin.

Other factors, however, did make a difference. As to the effects induced by American sugars, *T. effractum*, *T. plicatile*, *T. radiolatum* and *T. gypseum*, showed the same features as on "all French" mediums. *E. inguinale* showed changes of one or another sort but never so extreme but that enough characteristics remained to permit fairly ready and certain identification. With *M. lanosum* and *M. equinum*, the American sugars produced very marked variations, and these must be considered useless for purposes of universal identification.



Fig. 12.—Culture Series 3. *Microsporon lanosum*; colonies ten days old. Same test as Figure 11, except that only one control is shown at the left. Again the 10-90 combination of glucose and maltose (last tube) gives the closest approach to the control.

A few tests of American against French peptone were made on otherwise "all French" mediums, and notable and consistent differences noted with the two microspora, all in favor of the French peptone. As stated before, with the other five organisms the American was as useful as the French peptone.

The effect of this series, in respect to all seven organisms, was to show: (1) that we could use American agar, (2) that stoppers may be paraffined without detriment, (3) that the method of filtering was unimportant, (4) that the matter of peptone and maltose was unimportant with some of the fungi (the four trichophytons that we tested and *E. inguinale*), and (5) that *M. lanosum* and *M. equinum* were sensitive to all the different sugars and to peptone. This series had the effect of narrowing our further examinations to these two organisms

and of requiring for the present the use of French peptone with these. It is obvious that a synthetic American medium, to be of general value, must bring out the characteristics of every species, not simply the majority or any number short of 100 per cent.

Series 2.—This series, therefore, was carried out with only these two microsporons and on all the sugars used in Series 1. We have remarked before that we found the higher acidity of French medium was referable to the peptone in it, and we therefore tried to cover this point. We ran a series with (1) French peptone and (2) American peptone adjusted up to the French acidity with hydrochloric acid. The attempt was a failure because most of the adjusted tubes would not support growth; the organism could not stand it, and the occasional cultures which did develop did not compare at all with the "all French" control. Neither did any of the American sugars (we had tried only three in this respect in Series 1) when combined with French peptone agree



Fig. 13.—Culture Series 3. *Microsporon lanosum*; colonies seventeen days old, a little older than in Figure 8; corrected to + 1.8 with "hydrochloric acid albuminate" (in tubes where Difco peptone was used). Tube 1, "all French" control; Tube 2, "all French" R. A. L. maltose; Tube 3, "all French" except for American peptone; Tube 4, 50 per cent. dextrin—50 per cent. maltose; tube 5, 50 per cent. glucose—50 per cent. maltose; Tube 6, maltine; Tube 7, Difco. Tubes 1 and 5 are the most perfect agreements of all our five or six hundred trials. All the others in this picture have developed insufficient duvet—are too flat.

with the "all French." The effect of this series was (1) to indicate that free hydrochloric acid cannot be used as an adjuster, and (2) to confirm the impression that French peptone was essential.

Series 3.—In this series we proceeded along three lines. First, we adjusted acidity as in Series 2, but used an "acid albuminate" instead of free hydrochloric acid for adjusting. The acid albuminate was made by previously boiling decinormal hydrochloric acid with agar. The results were that, whereas this time growth took place freely enough on such adjustments, they did not compare in characteristics with colonies on French peptone or with the standard.

The second line in Series 2 was a rough preliminary test of synthetic mixtures of the probable ingredients of Sabouraud's maltose, i. e., dextrin, glucose and maltose, all chemically pure and American. French peptone was used with these. The combinations tried were: dextrin 100 per cent.; dextrin 90 per cent.—glucose 10 per cent.; dextrin 50 per cent.—glucose 50 per cent.; dextrin 10 per cent.—glucose 90 per cent.

Glucose 100 per cent.; glucose 90 per cent.—maltose 10 per cent.; glucose 50 per cent.—maltose 50 per cent.; glucose 10 per cent.—maltose 90 per cent.

Maltose 100 per cent.; maltose 90 per cent.—glucose 10 per cent.; maltose 50 per cent.—glucose 50 per cent.; maltose 10 per cent.—glucose 90 per cent.



Fig. 14.—Culture Series 3. *Microsporon lanosum*; colonies ten days old. Tube 1, "all French" control; Tube 2, "all French," except for Difco peptone (adjusted to + 1.8); Tube 3, "all French," R. A. L. maltose.

Results.—The nearest approach to the "all French" occurred in those tubes in which there was at least a notable quantity of glucose. One of the best reproductions occurred in the glucose 90 per cent.—maltose 10 per cent. combination.

Along the third line, we checked up and confirmed previous findings as to the effect of American and French peptone and agars.

The effect of this series was to indicate that acid adjustment alone would not bring the American peptone up to the French, and that therefore work would have to be further developed along this peptone line as well as along the maltose line. It also pointed to glucose as an essential carbohydrate in addition to the maltose, and appeared to exclude dextrin.

Series 4.—It then occurred to us that possibly the differing effects of American and French peptones were referable to a differing concentration of certain essentials, and that the American could be made to

approach the French by varying the quantity. Accordingly, graded concentrations of both French and American peptone were used, extending from 0.5 per cent. to 3 per cent.

Along the carbohydrate line, on the other hand, it was brought out in Series 3 that glucose induced a growth of mycelium particularly, resulting, as we desired, in a more hairy appearance than when maltose alone was used. This was particularly marked with *M. lanosum*. It was decided, therefore, to ascertain what effect the three carbohydrates (dextrin, glucose and maltose) would have in the absence of complicating peptone in bringing out the different units—the A. B. C's—which go to make up the characteristics of a culture. By units we mean such things as luxuriance, powderiness, moistness, hairiness, color, etc. Therefore the two microsporons were planted on American chemically pure glucose, dextrin and maltose, in the strength of 40 gm. of each,



Fig. 15.—Culture Series 4. *Microsporon equinum*; colonies fourteen days old; grown on graded concentrations of French and American peptone alone—no carbohydrates of any sort. Tubes 1 and 2 contain 3 per cent. peptone, French at the left, American at the right; Tubes 3 and 4, 1 per cent., French at the left, American at the right; Tubes 5 and 6, peptone, 0.5 per cent., French at the left, American at the right. The proper wooliness was not elicited by any American concentrations tried, and not in weaker French concentrations (0.5 per cent.).

separately, per 1,000 cubic centimeters. The results were most striking. In the case of the peptone cultures, hairiness developed only in the 2 per cent. and 3 per cent. French peptone mediums. All the others were moist, even the 3 per cent. American peptone. The bulk of growth was quite satisfactory on the 3 per cent. American peptone.⁷

The growths on the three sugars showed no hairiness whatsoever. It was only possible to see the colony by slanting the tube in the most advantageous light, and then the surface growth was discovered to

7. In all American tubes the organism extended deeply into the medium. This was particularly the case with the weaker concentrations.

consist of translucent filaments which crept closely over the surface. That is, the sugars were conducive to a flat, translucent, moist type of colony.

The general effect of both these tests was to show that the course of studies toward eliciting wooliness lay in some other direction than the sugars and the American peptone. In this connection we have noted for a long time that the French peptone appears much cruder than the American. It has a distinct yellow color and comes in coarse granules. No doubt there are nitrogenous or other impurities intermixed in it which are responsible for the wooly appearance. These are the sub-

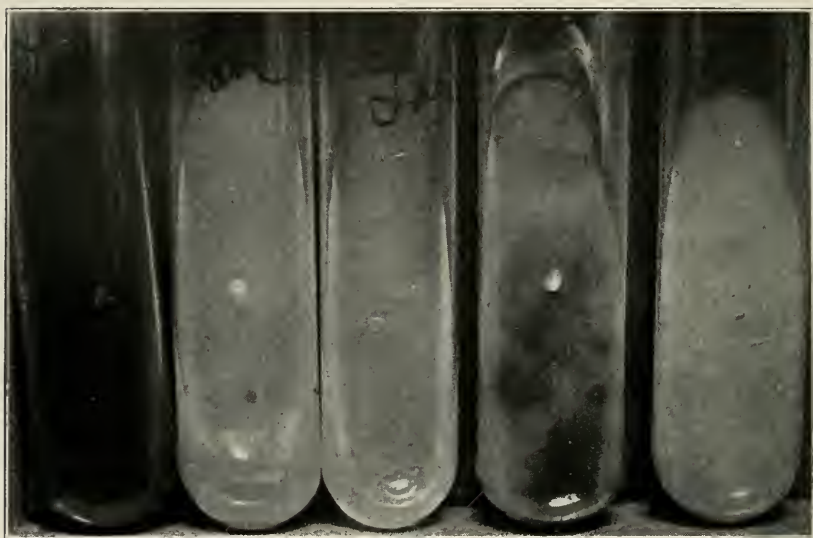


Fig. 16—Culture Series 4. *Microsporon lanosum*; colonies fourteen days old; on chemically pure carbohydrates only (4 per cent.)—no peptone. Tube 1, French maltose; Tube 2, French glucose (masse); Tube 3, American glucose (Mulford); Tube 4, American dextrin (Merck); Tube 5, Difco maltose. There are scanty surface growths on all tubes, but they are moist and translucent, and do not photograph well. The darker color of tube 4 is due to its red color.

stances which should be logically intermixed (amino-acids such as tryptophan, and possibly urea, phosphates, ammonia salts, etc.) in any further attempts at synthesizing an American medium comparable to Sabouraud's proof medium, a ponderous and unpromising prospect indeed. Certainly we have been obsessed by the maltose factor of the proposition and have been neglecting the nitrogenous and inorganic salt phases.

Just as we were completing the last set of tests we received word from Sabouraud that the original crude maltose was no longer obtainable and that glucose agar was as useful as maltose agar. This was

a surprise, in view of the impression we have gained from Sabouraud's book; and clearly this course has been forced on French mycologists as a result of French conditions.

CONCLUSIONS

1. Only certain species of molds (probably a very small number indeed) require crude French maltose and French peptone for identification. With many, American chemically pure (Difco) products serve perfectly well and no adjustment of reaction is necessary.

In respect to the "maltose-sensitive" organisms:

2. In the present state of the French maltose market and the absence of substitutes, we shall have to depend on glucose agar.

3. Imported French peptone (Chassaing) must be used.

4. American agar may be used, and either American cotton or filter paper used for filtering.

5. No adjustment of reaction is necessary as this is taken care of by the French peptone.

6. There is no American maltose, either chemically pure or crude, that can be substituted for the original article. The recently recommended R. A. L. imported French sugar will not serve. This has been confirmed by Sabouraud in a personal communication.

7. American peptone (Difco) must not be used.

SIGNIFICANCE OF RESULTS

What does all this mean in relation to the general broad proposition of ringworm culture? We refer to methods which always have been uncertain and unsatisfactory, and are now even more so, with the present lack of French maltose. We have intimated before how variable the composition of the original "proof" medium was, composed as it was of biologic ingredients whose composition may vary from time to time. Even if the original French maltose should again become available, we should be no better off, for there is no guarantee that it would be the same 100 years from now. The same is true of the French peptone. Methods of manufacture could change during that time, firms go out of business, etc.

It means, then, this: The consummation devoutly to be wished is a new medium composed of definite, chemically pure ingredients, of reasonable cost, adjusted to a standard acid figure, which will approach as closely as possible Sabouraud's pictures. Something of this sort is quite necessary as a permanent foundation for the study of such pleomorphic, protean organisms as these molds.

This is an exacting and radical proposition, but such surgery often proves to be best in the long run. It would undoubtedly involve the abandonment of Sabouraud's maltose characteristics—really, they are

done for now—and doubtless some modification of the glucose figures of some of the molds. It would not mean that the whole of the gross morphologic chapter would have to be rewritten, and of course it would not involve the clinical, statistical or microscopic sections of his book.

Anything short of a new culture medium would be only perpetuating the unsatisfactoriness of the original "proof" medium. As seen at present, chemically pure glucose promises best and will doubtless be perfectly satisfactory on the carbohydrate side. A modified Raulin's fluid should be kept in mind from the nitrogenous side, etc., and may some day prove useful in place of peptone, somewhat as follows:

Tartaric acid.....	4 gm.
Ammonium nitrate.....	4 gm.
Ammonium phosphate.....	0.60 gm.
Potassium carbonate.....	0.60 gm.
Magnesium carbonate.....	0.40 gm.
Ammonium sulphate.....	0.25 gm.
Zinc sulphate.....	0.07 gm.
Iron sulphate.....	0.07 gm.
Potassium silicate.....	0.07 gm.
Water	1,500 c.c.

This was originally recommended for growing *Aspergillus niger*. Work along this line remains to be done.

As the ringworm culture problem stands today, we recommend that Sabouraud's maltose characters be abandoned and that the work be pursued on glucose mediums made from American ingredients, with the exception of the peptone. This must be French (Chassaing).

TABLE 2.—INDEX OF INFORMATION BROUGHT OUT BY THE ILLUSTRATIONS

1. Adequacy of certain American maltoses for "maltose-insensitive" species. Figures 1 (in part—[Pfanstiehl and Mellin's]), 2, 3 and 4.
2. Inadequacy of American maltoses for "maltose-sensitive" species. Without acid adjustment, Figures 1 (in part) and 5. Also with acid adjustment, Figures 6, 8 and 13.
3. Necessity for French peptone. With no acid adjustment, Figures 1, 4 and 5. Even with acid adjustment, Figures 13 and 14. (At least desirable if not "necessary" in the case of Figure 4.)
4. Uselessness of proposed French maltose substitute R. A. L. Figures 7 and 14.
5. Effect on morphology of graded amounts of peptone, both American and French—no carbohydrate. Figure 15.
6. Effect on morphology of carbohydrates alone—no peptone. Figure 16.
7. Suitableness of American agar. Figures 1 and 3.
8. Non-importance of filtering methods. In Figures 1 and 4, Tube 1 was filtered through French filter paper, Tube 3 through American filter paper, and Tube 4 through cotton.
9. Nonimportance of paraffining stoppers. In both Figures 1 and 4, Tubes 1 and 3 were paraffined, while Tubes 4 and 5 were not.

POROKERATOSIS

REPORT OF A CASE *

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In 1893 Mibelli ¹ and Respighi ² simultaneously called attention to a form of dermatosis not previously described. To this condition Mibelli gave the name of "porokeratosis," while Respighi termed it "hyperkeratosis eccentrica." During the twenty-seven years that have intervened since the first description of this affection, not over sixty cases have been reported in the literature. In this country in particular the condition is extremely rare, cases having been published only by Hutchins, Gilchrist, Wende and Heidingsfeld. Since 1898 no authentic case of porokeratosis occurring in the United States has been reported, Heidingsfeld's in 1905 only simulating the condition histologically. The following case was seen recently in this hospital.

REPORT OF CASE

History.—The patient, a Greek, 40 years old, entered the dermatological service of the University Hospital because of lesions on the hands, buttocks, legs and feet. He described lesions corresponding exactly to those he presented as occurring on the hands and feet of his father, and said that the father told him that the grandmother had had the same condition. The father told him also that it was a family disease occurring throughout the life of those affected, all efforts toward a cure being useless. Although the patient said that his wife and four of his children were entirely free from lesions of any kind, a fifth child, a girl 9 years old, had warty appearing elevations on one leg. The patient gave an indefinite history of having had a soft, painful, penile lesion at the age of 15. This was accompanied by an eruption over his body, the details of which he had forgotten.

The lesions which he presented had been present since infancy. The exact date of their appearance he does not know, but was told by his father that his feet were first affected, when he was but 1 or 2 years old. Later, new lesions appeared on the scrotum, buttocks and penis, and finally on the hands and present sites of election. He described them as appearing first as small brownish

* Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

1. Mibelli: Contributo allo studio della ipercheratosi dei canali sudoriferi, Gior. Ital. d. mal. ven. 1893, p. 313; Beitrag zum Studium der Hyperkeratosen der Knaueldrüsen ganges, Monatsch. f. prakt. Dermat. **17**:417, 1893, translation of (1).

2. Respighi: Di una ipercheratosi non ancora descritta, Gior. ital. d. mal. ven. 1893, p. 356; Ueber eine noch nicht beschriebene Hyperkeratose, Monatsh. f. prakt. Dermat. **18**:70, 1894.

spots which, increasing in size, became depressed in the center. They were accompanied by a severe pruritus. It was this subjective symptom that brought the patient to the hospital.

Examination.—The patient was a well nourished man of fair appearance. His scalp was clean. The pupils were equal and reacted to light and accommodation. There was slight axillary and inguinal adenitis; the spleen and liver were not palpable, and the heart and lungs were normal. The reflexes were present and equal. The blood Wassermann reaction was negative.

Back of the left ear, on the forehead, neck, hands, buttocks, scrotum, feet and legs were about twenty raised, verrucous lesions. These varied in size from those a few millimeters in diameter to some as large as a dollar. For the most part they were noninflammatory, but on the scrotum and in the peri-anal region they were mildly inflamed and slightly eroded. The smallest lesions were barely visible and presented themselves as brownish, slightly elevated papules. These were found chiefly on the forehead and back of the ear. Lesions about a centimeter or more in size presented a distinctly verrucous appearance, and in the instances of the older ones showed a raised, wavy border and a depressed center. Lesions of this type were entirely confined to the feet. Examination of the border of the lesion revealed a shallow groove running around the summit, this groove being slightly overlapped by a flap of its internal wall. The height of this border varied from 1 mm. to 5 or 6 mm. The depressed center presented itself as a smooth, callous surface, showing entire absence of hair follicles and having a brownish pigmentation. There were definite scratch marks over some of the lesions. The palms and soles were free and the nails were not affected.

Microscopic Examination.—In order to make a complete pathologic examination of this condition, it was thought necessary to study lesions in various stages. For this purpose, five lesions were excised, varying from the smallest demonstrable papule to the larger, ringed patches. The tissues were fixed in formol and in alcohol, imbedded and cut in paraffin. In making the stains hematoxylin and eosin, toluidin blue, Unna's polychrome methylene blue, neutral orcein and Pappenheim's stain were employed.

The first sections studied were cut from a lesion about 2 mm. in diameter, excised from the forehead. A portion of the surrounding skin was taken for comparison. The process at this stage showed an acanthosis, accompanied by a slight degree of hyperkeratosis. The horny layer for the most part was composed of cells with indefinite outlines and well-stained, shrunken nuclei. There was considerable scale formation. The entire thickness of the stratum corneum was slightly less than that of the underlying stratum granulosum, which was composed of from three to four layers of cells. The stratum lucidum was wholly undemonstrable. The hair follicles were distended and filled with horny material which stained deeply with eosin. Other horny plugs could be traced through serial sections to the sweat ducts, but these were by no means prominent. The acanthosis resulted from a thickening of the prickle cell layer. This layer showed in its central portion many distended and separated cells. The basal columnar layer of cells was unchanged. One of the most striking features of the early stage was the marked prolongation of the interpapillary tufts deep into the cutis. The cutis also shared considerably in the changes. The capillaries show dilatation and were surrounded by collections of lymphoid cells. The infiltration of these cells was most marked in the center of the lesions, large collections being found around the hair follicles. There were only few sweat gland ducts visible in the corium.

The second piece of tissue studied was a slightly larger lesion than the first. It showed no increase in the acanthosis, but a distinct increase in the hyperkeratosis over the earlier lesions. The stratum corneum here was made up of from ten to twenty layers of cells, being thickest in the region of the follicles and orifices of the sweat glands. The cells had fairly definite outlines and well stained shrunken nuclei as in the first section. Projecting down into the distended openings of the follicles and sweat ducts were definite conical plugs made up of cells, some of which were entirely cornified, while others showed definite nuclei. The marginal cells of these plugs mingled with those of the hyperkeratotic stratum corneum. Throughout the stratum corneum there were inclusions of hyaline pink-staining material and numerous minute abscesses. The stratum granulosum was thinned out except in the region of the follicles, where it was composed of from three to four layers of cells. The stratum lucidum was again invisible. The cutis showed capillary and lymph space dilatation and considerable round cell infiltration. Here again there was no demonstrable change in the ducts of the sweat glands, but there were few of these in the section. Unfortunately, this bit of tissue was not excised deeply enough and extended but a little distance below the papillary layer of the corium.

The third section was taken from the leg and was the largest section, showing no central depression. The hyperkeratosis here was equal to the acanthosis. It was more compact, and no cell outlines or nuclei were to be seen. The same was true of the hyperkeratosis in the follicular openings. The plugs were very compact and penetrated deeply into the follicles. The stratum lucidum was thickened and distinctly visible. The stratum granulosum in places consisted of from six to eight layers of cells. In the corium there was more marked dilatation of the lymph spaces and capillaries than in the previous sections and a marked edema. In some places the walls of the blood vessels showed endothelial proliferation. There was also some dilatation of the sweat ducts. The picture was much the same as that of a verruca.

The fourth and fifth pieces of tissue were taken from lesions which macroscopically showed the raised peripheral wall with its characteristic crater and depressed center. The wall in the first of these lesions was only slightly elevated, while in the second it was about 5 mm. in height. The central area showed a much thinned out epidermis, and the hyperkeratosis was much less marked, although very compact. There was a total absence of hair follicles and sebaceous glands in this depressed center, but an occasional sweat duct was visible. The peripheral wall was formed by the markedly thickened stratum corneum and the hyperacanthosis of the prickly cell layer. Over the seam of the wall the hyperkeratotic tissue showed many well stained, atrophic nuclei. At no other places in the stratum corneum were they visible. By studying serial sections, numerous sweat ducts could be seen to converge toward the seam of the peripheral wall. These ducts were somewhat dilated, and the horny plugs reached down into their orifices. The cutis showed an increase in the collagen. The cellular infiltration was most marked beneath the wall.

REVIEW OF THE LITERATURE

In 1887, Domenico Majocchi observed a case of the affection in a 15-year old boy. He did not recognize its nature and presented it to his pupils at the University of Parma as a case of *ichthyosis hystrix*. At that time a photograph was made of the lesions on the forearm of

the patient and presented to the Institute of Dermatology at Parma. Six years later the same boy was seen by Mibelli,¹ who recognized the lesions as exceptional and different from the condition previously recorded. This case with two others he reported in the Italian literature, giving a full description of clinical and histologic findings, together with a résumé of previously described entities with which the condition could be compared. The picture, as Mibelli presented it, consisted of lesions beginning as warty, dry, cone-shaped elevations less than 1 cm. in diameter, which spread peripherally, leaving a depressed, dry, callous center. The border took on special characteristics unlike those of any other disease. Mibelli described it as having the appearance of a dyke



Fig. 1.—Typical lesions of porokeratosis, showing peripheral wall and central depression.

with a shallow central depression at its summit. In one instance a lesion reached such a size that the entire forearm and hand were covered. There was a predilection for the hands, face, genitals, legs and feet. Mibelli designated the disease as an essentially chronic one, beginning in the earliest years and continuing throughout the life of the patient. Attention was called by him to the hereditary tendency of the condition. As an example, he mentioned that two of his cases occurred in brother and sister.

In making a histologic study, the youngest lesion excised was two years old. Mibelli stated that the disease began as an acanthosis of the

surface epithelium, accompanied by a hyperkeratosis. In an advanced stage the hyperkeratosis stopped and there was an atrophy of the prickle cell layer through pressure of the already formed keratoma. In these places the hair follicles and sebaceous glands were absent. The process affected chiefly the sweat gland pores, which were filled with a horny black layer. The center of the duct projected out like a plume. It was by a coalescence of a number of these plugs that the ridge was formed which distinguished the advancing border of the affection. In the cutis there was a dilatation of the vessels of the papillary and sub-papillary parts. About the walls of the vessels there was an infiltration of lymphoid cells. In no place was there migration of these cells into the interspinous spaces of the prickle cell layer. The most important changes Mibelli believed to be in the coil of the sweat gland and its outlet. Where the interepidermal part of the duct was still patent, for the most part, notwithstanding keratinization, the coil still retained its normal dimensions but was deformed by localized dilatations which in some instances looked like cystic enlargements. Its epithelium was much reduced and compressed. In later stages new collagenous tissue appeared between the loops of the coils and gradually led to atrophy. The rest of the cutaneous tissue also atrophied, leading to central depression.

Respighi's² simultaneous article in the same journal contained a report of seven cases. He termed the affection "hyperkeratosis eccentrica" and divided the lesions into five distinct forms: (1) miliary to (2) lentil to (3) guttate-sized papules, (4) ringed lesions with a wall and a central clear space, and (5) cone or shell-shaped papules found only on the tips of the toes. He found that the nails were secondarily affected and described them as cloudy, brittle and falling off easily. Spots were found on the palms and soles.

The histology in these cases followed closely that of Mibelli, but more stress was laid on the involvement of the follicles with horny plugs which penetrated almost to the acini. Respighi found that the marginal wall was formed by the hyperkeratosis combined with thickened papillae. It was his idea that there was a parasitic hyperkeratosis or parakeratosis of the mouths of the tubular and acinous glands.

In the following year an attempt was made by Tommasoli³ to prevent the recognition of porokeratosis as a distinct type of dermatologic affection. Without personally observing the cases, he maintained that the term porokeratosis was quite superfluous, as there were several forms of keratodermatitis attended by marked keratotic changes in the

3. Tommasoli: Sulla nuova ipercheratosi recentemente studiata dal Professor Mibelli e dal Dott. Respighi, *Comment clin. d. mal. cut. e gen. ur.*, 1894, No. 1.



Fig. 2.—Typical late lesion, showing crater at the summit of the peripheral wall.

glandular follicles, particularly of the sweat glands, which, even if less marked than in porokeratosis, could be attributed to their relatively shorter duration. He placed the affection under the classification of the pseudolichens and suggested the name of "circinate pseudolichen porokeratosis." It was Tommasoli's idea that there was an autotoxic etiology for the condition.

In response to this article, Mibelli⁴ published a lengthy refutation in which he insisted that the clinical and histologic characteristics of the disease described simultaneously by himself and Respighi were entirely different from any other condition. He states that the presence of keratosis in the gland ducts in other conditions, such as Darier's disease, pityriasis pilaris and lichen planus, was merely an associated finding and not the preponderating cause.

Respighi,⁵ in 1895, having seen his eighth case, published a new work in which he discussed his attempts to prove that there was a

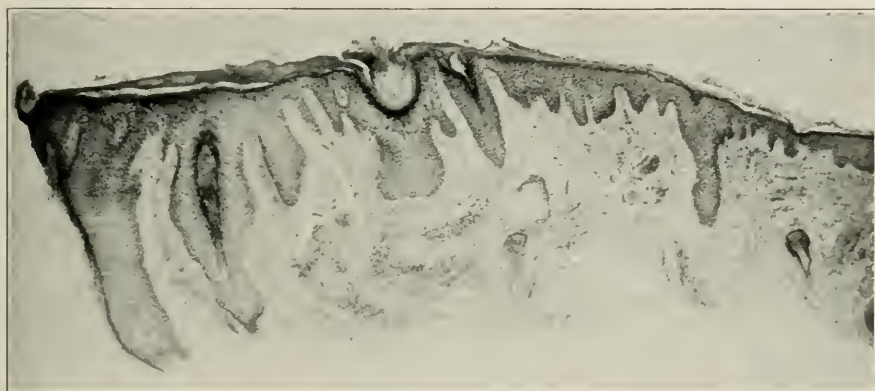


Fig. 3.—Biopsy of smallest demonstrable lesion, showing hyperkeratosis, plug in hair follicle, acanthosis, thickening and dipping down of interpapillary tufts and inflammatory reaction in the corium.

parasitic cause, and his negative results. In this article he stated that he refused to accept the hypothesis of Mibelli that the condition results from an alteration of the sweat apparatus, and held that Tommasoli's suggestion of its being an autotoxic keratodermatitis was untenable. The fairly definite family history would preclude the latter theory.

4. Mibelli: Sulla porokeratosi: a proposita di una critica, *Gior. ital. d. mal. ven.* 1894; Ueber die Porokeratose, *Monatsh. f. prakt. Dermat.* **20**:309, translation of (6).

5. Respighi: Sulla iperkeratosi eccentrica, *Gior. ital. d. mal. ven.* **1**:69, 1895; *Brit. J. Dermat.* **7**:1895; Ueber die Hyperkeratosis Excentrica: *Monatsh. f. prakt. Dermat.* **21**:499, 1895, translation of (8).

In response to this second article of Respighi's, Mibelli ⁶ insisted on the interpretation he had before given, and the title of "porokeratosis." At the meeting of the Italian Society of Dermatology and Syphilology in October, 1895, the question was discussed pro and con by the two men; Respighi ⁷ at that time presented three new cases, showing photographs and histologic preparations. At this meeting Majocchi expressed his opinion that the disease was a hyperkeratosis of the gland pores, but he considered it a variety of ichthyosis in which hyperkeratosis of the gland ducts predominated.

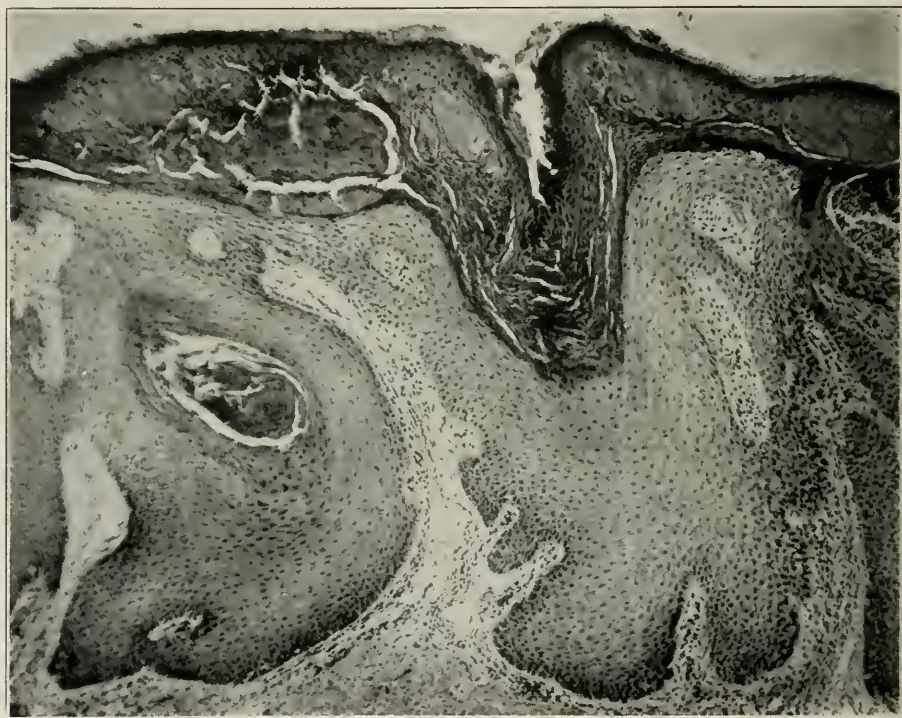


Fig. 4.—Biopsy of larger verrucous lesion. Marked hyperkeratosis, plug in follicle and acanthosis.

Later, in a report presented to the International Congress on Dermatology in London (Aug. 1, 1896), Mibelli ⁸ stated that the kera-

Mibelli: Iperkeratosi Eccentrica. Duex mots de response au Dr. Respighi, *Gior. ital. d. mal. ven.* **2**: 1895.

7. Respighi: Di una singolare ipercheratosi, *Gior. ital. d. mal. ven.* **2**: 1896, (communication to the annual reunion of the Italian Society of Derm. and Syph., held at Rome in October, 1895).

8. Mibelli: L'etiologia e le varietà delle cheratosi, *Gior. ital. d. mal. ven.* **4** and **5**: 1896.

otic cone was never seen in a follicular orifice, but always in a sweat gland orifice, and that the hyperkeratosis occurring in a follicular orifice did not resemble in color, form, structure or development that found in a sweat pore.

About this time the first case was reported in America by Hutchins.⁹ In his patient the disease began at the age of 2 on the palms and spread peripherally. The family history was negative. Clinically the condition corresponded to Mibelli's description, except for the subjective symptom of itching. Unfortunately, Hutchins was unable to



Fig. 5.—Cross-section of plug deep in epidermis, inflammatory reaction in papillary and subpapillary layers of cutis.

obtain any sections for histologic study. Because of the involvement of all of the epithelial structures, he suggested the name of "panokeratosis or poropanokeratosis." To him goes the credit for reporting the first case seen in this country, although Stelwagon in his treatise on dermatology tells of a case seen by him in 1887, the true nature of which he did not recognize until some years later.

9. Hutchins: A Case of Porokeratosis Mibelli, *J. Cutan. Dis.* **14**: 1896.

At this point it would be most logical to mention the later American reports. The second report to be published in this country was that of Gilchrist¹⁰ in 1897. His patient, a man 21 years old, had had the disease since the age of 5. In the same family Gilchrist traced eleven cases of the affection, thus giving ample proof of the hereditary tendency. In experiments with various forms of treatment he obtained good results with excision and with actual cautery, but found that recurrence took place following curettement and application of silver nitrate.

Wende,¹¹ in 1898, saw a single lesion in a woman, aged 45 years. It had begun at the age of 45 as a small, rough, scaly plaque between the thumb and finger of the left hand. After a year of quiescence it began to spread peripherally and became depressed in the center. It was accompanied by a severe pruritus. Histologically, he found the stratum lucidum to be barely visible, but the stratum granulosum was hypertrophied, especially near the sweat ducts. Thirty attempts at inoculation were unsuccessful with the exception of one instance in the original patient in which a lesion appeared accompanied by marked itching and histologically corresponding to porokeratosis. The patient, fearing the development of a second patch like the original, insisted on early excision of the experimental lesion.

Heidingsfeld,¹² in 1905, reported a case in the American literature of a man, aged 26, who for eight years had had an eruption of the left leg, the affected area presenting a pinkish-white color, somewhat sclerotic and studded irregularly with numerous small, rounded, keratotic elevations somewhat larger than pinheads. From the clinical examination a diagnosis of lichen chronica circumscripta was made, but histologically a marked plugging of the sweat pores was observed, which prompted a diagnosis of porokeratosis. Other than the one feature—the plugging of the sweat pores—this case has none of the features of porokeratosis, either macroscopically or microscopically, and undoubtedly is not a true Mibelli's disease. Heidingsfeld made a histologic study of many other conditions, and a similar plugging of the ducts was found in pityriasis rubra pilaris, prurigo, ichthyosis hystrix, clavus, linear nevus and generalized papular dermatitis.

The reports of Hutchins, Gilchrist, Wende and Heidingsfeld complete the bibliography of porokeratosis in the literature of this country,

10. Gilchrist: A Case of Porokeratosis (Mibelli) or Hyperkeratosis Eccentrica (Respighi) with a Remarkable Family History. Preliminary Notice, Johns Hopkins Med. Bull. **74**: (May) 1897; Eleven Cases of Porokeratosis in One Family, J. Cutan. Dis. **17**:149, 1899.

11. Wende: Porokeratosis with Report of a Case, J. Cutan. Dis. **16**:505.

12. Heidingsfeld: Porokeratosis Mibelli, J. Cutan. Dis. **24**:29, 1905.

with the exception of one or two publications of foreign writers which will be mentioned later. There is a photograph in Ormsby's¹³ "Diseases of the Skin," taken from a case of Montgomery, but no report of this case is made in the literature.

Reisner¹⁴ observed a seasonal variation in the case which he discussed at the inaugural dissertation of the Medical Faculty of Strassburg in 1896. He observed that the lesions were accentuated in summer and attenuated in winter. That there was a true atrophy of the sweat

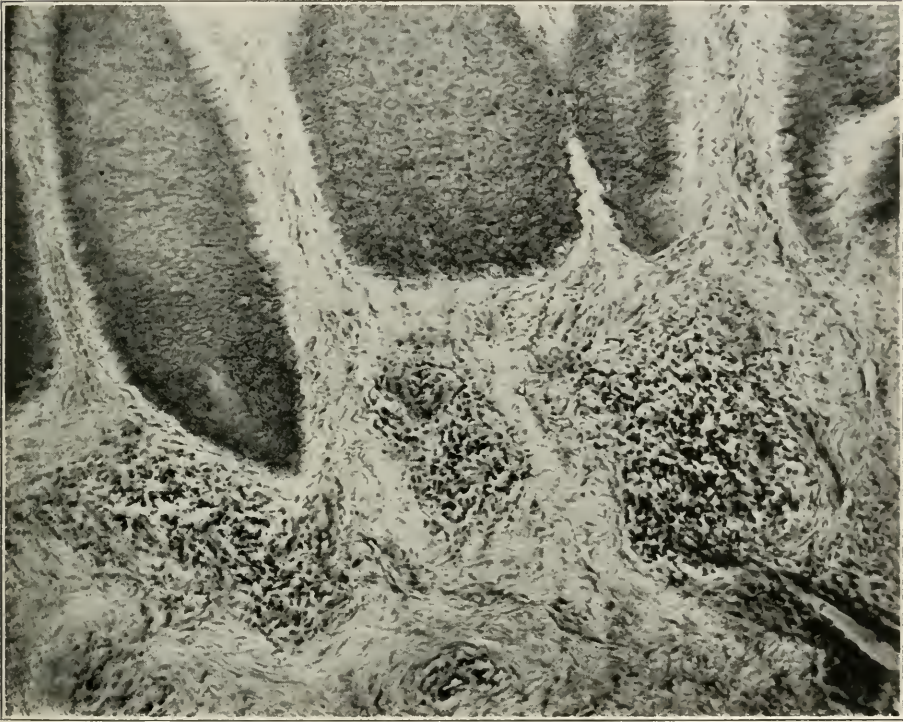


Fig. 6.—Collections of lymphoid cells in subpapillary layer of cutis.

glands in the depressed center, he proved by the fact that sweating was not produced by the administration of pilocarpin.

The first distinct variation in the histology of the condition was brought out in the cases of Joseph.¹⁵ The disease began in the two patients at the age of 3 and 8 years, respectively. He found microscopically that the stratum granulosum was only one or two cells in

13. Ormsby: Diseases of the Skin, Rev. Ed., Philadelphia, Lea & Febiger.

14. Reisner: Ein Fall von Porokeratosis, Inaug. Dissertation von der Medic. Fac. Strassburg, 1896. (Quoted from Respighi).

15. Joseph: Ueber Porokeratosis, Arch. f. Dermat. u. Syph. **39**: 1897.

thickness. In the corium, between the coils of the sweat glands, the mast cells were increased in number and in the epithelium of the glomeruli were numerous karyokinetic figures. He explained these differences from the histology as described by Mibelli as due to the fact that his patients had had the disease only a few years while Mibelli's patient had had it for many years. Mibelli, in a later article, was not inclined to view Joseph's case as a true porokeratosis.

Ducrey¹⁶ and Respighi, at the meeting of the Italian Society of Dermatology and Syphilology in Rome in 1897, announced that they had observed three cases of the disease in which the lesions were on the buccal mucosa. Clinically and histologically these lesions corresponded exactly to those present on the skin except for modifications due to differences in the tissue affected.

Basch,¹⁷ in 1898, reported the case of a man, aged 36, who had had the lesions since the age of 10. Although patches were found on the mucous membrane, they were not studied microscopically. From the histologic study of the skin lesions, the author concluded that the process had its beginning in the epidermis, agreeing with the views of Mibelli, Reisner, Joseph and Gilchrist. A marked degree of pruritus was the only subjective symptom.

Respighi¹⁸ and Ducrey, in a joint monograph, reviewed the former's eleven cases and gave an exhaustive account of the report of other authors. In all of Respighi's patients the skin was affected, in five alone and in six simultaneously with the mucous membranes. In no case was the affection limited to the mucous membrane. The tendency of the disease to appear in several members of the same family was marked in their observations. In only two cases of the eleven did the condition appear in virgin soil, while the remaining nine cases were gathered from three families—two, three and four cases, respectively, from each. Outside of the cases seen and examined personally by the writers, the first family had eight more members similarly attacked, the second and third families one more in each. In no case was the disease transmitted from husband to wife. In the first family all four members were nursed by the same woman. In the lesions on the mucous membranes they found a ridge surrounding a central area, in

16. Ducrey and Respighi: Les localizations sur la muqueuse bucale de l'affection improprement appelée porokeratose, communication to the Ital. Society of Dermat. in December, 1897, published in *Annal. de. Derm. et de Syphiligraph*, January, 1898, p. 1.

17. Basch: Ein fall von Porokeratosis (Mibelli). *Pest. med. chir. Presse*, **34**:27, 1898.

18. Ducrey and Respighi: L'Hyperkeratose Figurée Centrifuge Atrophiante, *Ann. d. Dermat. et Syph.* **9**:609 and 734, 1898.

this way corresponding to skin lesions. However, they described the ridge of the mucous membrane patch as being very thin and never showing a seam in its center. Histologic study of the skin lesions showed that the central area was occupied by the opening of a tubular or acinous gland, by a hair follicle and its sebaceous appendage, or no gland at all was present. The raised seam was formed by modified cells of the malpighian layer and subjacent connective tissue. Respighi and Ducrey thought that the disease might have its origin in the corium rather than in the epidermis. Because of the exceptional clinical char-

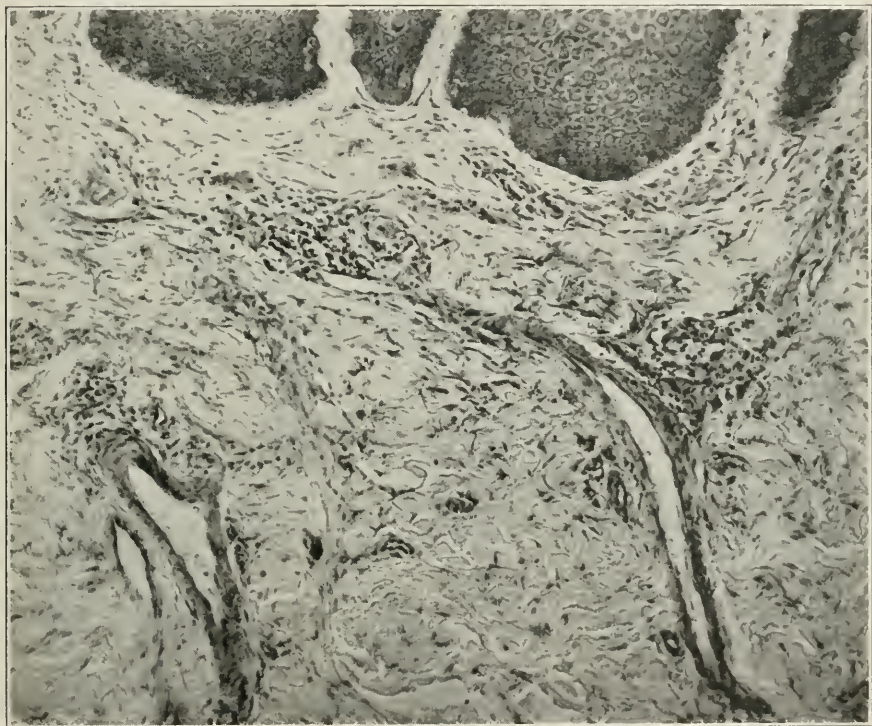


Fig. 7.—Dilated lymph and blood spaces surrounded by lymphoid cells.

acteristics they suggested the name "hyperkeratosis figurata centrifuga atrophicans" instead of "porokeratosis."

Mibelli,¹⁹ in 1899, reported a case in which lesions were found on the glans penis and in the mouth in a patient 68 years old. The disease was of thirty years' duration and occupied the trunk and both extremities. It was traceable through four generations.

19. Mibelli: Ueber einen Fall von Porokeratosis mit Localization in Munde, Arch. f. Dermat. u. Syph. **47**:1, 1899.

Heller,²⁰ in a report of a single case, told of marked improvement following the use of a salicylic acid and mercury plaster.

The lesions in Wolf's²¹ case were absent in winter and appeared each summer.

Between the years of 1900 and 1905 there was very little published concerning porokeratosis. A case of Du Castel and Langlet²² was thought to be lichen planus by Hallepeau and Darier, the former basing his opinion on the clinical picture and the latter on the histologic findings. Typical lesions of lichen planus were found on the forearms and glans penis. Galloway²³ saw the disease in a girl, aged 17, but made no histologic study. Mantoux's peculiar form of keratosis of the palms and soles, which he entitled "porokeratose papillomatose" had nothing to do with the sweat ducts microscopically, and clinically was not a case of true porokeratosis Mibelli.

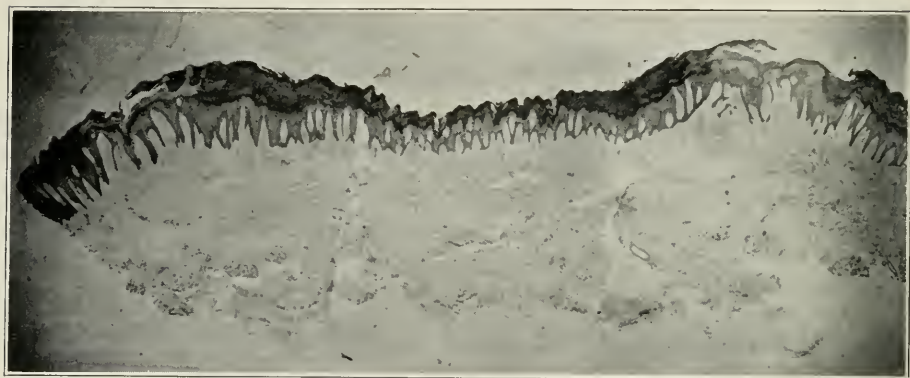


Fig. 8.—Late lesion showing depressed center and peripheral walls with depressions corresponding to craters; absence of sweat ducts and follicles in central area; hyperkeratosis, plugging of sweat ducts, acanthosis and inflammatory reaction in cutis in the region of the peripheral wall.

Mibelli,²⁴ in 1905, reported two new cases. The first occurred in a man of 66 and had been present since early life. The second occurred

20. Heller: Demonstration of a Case, *Verhandlung Berl. Dermat. Gesellsch., Dermat. Ztsch.*, 1899, p. 671, and *Arch. f. Dermat. u. Syph.* **47**:435.

21. Wolf: Demonstration of a Case of Porokeratosis, *Arch. f. Dermat. u. Syph.* **47**:415, 1899.

22. Du Castel and Langlet: Porokeratose, *Soc. de dermat., February, 1900; Ann. de dermat. et syph.*, 1900, p. 228.

23. Galloway: Case Demonstration, *London Dermat. Soc., Brit. J. Dermat.*, 1901, p. 262.

24. Mibelli: *Le propos. de deux nouveaux cas de Porokeratose*, *Ann. de dermat. et syph.*, 1905, p. 503.

in a man of 20 and had been present for ten years. His grandfather, father, uncle and two brothers also were affected with the condition. Mibelli places the disease among the incurable dermatoses.

Truffi,²⁵ writing in the same number of the *Annales*, reported a case in a boy of 13 in whom the lesions had been present since the age of 11 months. In this patient there was a definite grouping of the patches, corresponding to the distribution of peripheral nerves to the affected areas. Thus, he found that a lesion on the face was exactly limited by the median line and occupied, as adjacent patches, the areas innervated by the last two branches of the trigeminal nerve. In this way, the entire eruption could be mapped out according to nerve distribution. Mibelli²⁶ confirmed Truffi's case to be a true porokeratosis, and in a later article referred to it as a point of confirmation of his first opinion—that porokeratosis should be regarded as a disease beginning in the superficial layers of the skin and having its seat in an alteration of congenital origin. He refers to Truffi's case because of the systematic arrangement, which is common with nevi.

In 1907 cases were reported by Himmel²⁷ and Brocq and Pautier.²⁸ The former made a necropsy examination of a case in which the patient died of an intercurrent affection, but was unable to add anything to the knowledge of the condition. The case of the two latter men lacked the seam in the peripheral wall of the lesions, which is one of the chief characteristics of a true Mibelli's porokeratosis. Baum,²⁹ in 1908, saw lesions distributed along the nerve trunks, and while the case was under observation a new nerve was affected.

Pasini,³⁰ in 1912, before the International Congress of Dermatology gave a report of twenty-six cases being found in one family. Maki,³¹ a Japanese observer, was reminded of systematized nevi by the localization of three cases of this disease. The first two cases occurred in brothers and affected the face, neck, back and legs symmetrically in

25. Truffi: Sur un cas de Porokeratose systematisee, *Ann. de Dermat. et syph.*, 1905, p. 520.

26. Mibelli: A propos. de l'article de Truffi "Sur un cas de porokeratose system," *Ann. de dermat. et syph.*, 1905, p. 595.

27. Himmel: Ein Fall von Porokeratosis, *Arch. f. dermat. u. syph.* **84**:279, 1907.

28. Brocq and Pautier: Cas de Porokeratose, *Bull. Soc. Hôp. de Paris*, January, 1907, p. 651.

29. Baum: Porokeratosis Mibelli, *Verhandlung Deutsch. Dermat. Gesellsch.*, June, 1908, *Arch. f. dermat. u. syph.* **91**:363.

30. Pasini: Demonstration VII International Dermat. Congress, Rome, *Dermat. Wehnschr.* **55**:1733, 1912.

31. Maki: Three Interesting Cases of Porokeratosis and Its Treatment, *Abst. in J. Cutan. Dis.*, July, 1914; *Japan Ztsch. f. Dermat. u. Urol.*, January, 1914.

both. The third was in a girl, the side of the head being affected. Treatment with roentgen ray, radium, mesothorium, quartz-lamp and carbon dioxid snow was tried out. The best success was attained by the last.

Isaac³² demonstrated a case in 1913 in which only the scrotum was involved

Matosumoto,³³ in 1917, reported a case of lesions on the hand in a man, aged 27, consisting of minute horny, conical elevations and slight depressions with comedo-like plugs, which histologically showed hyper-

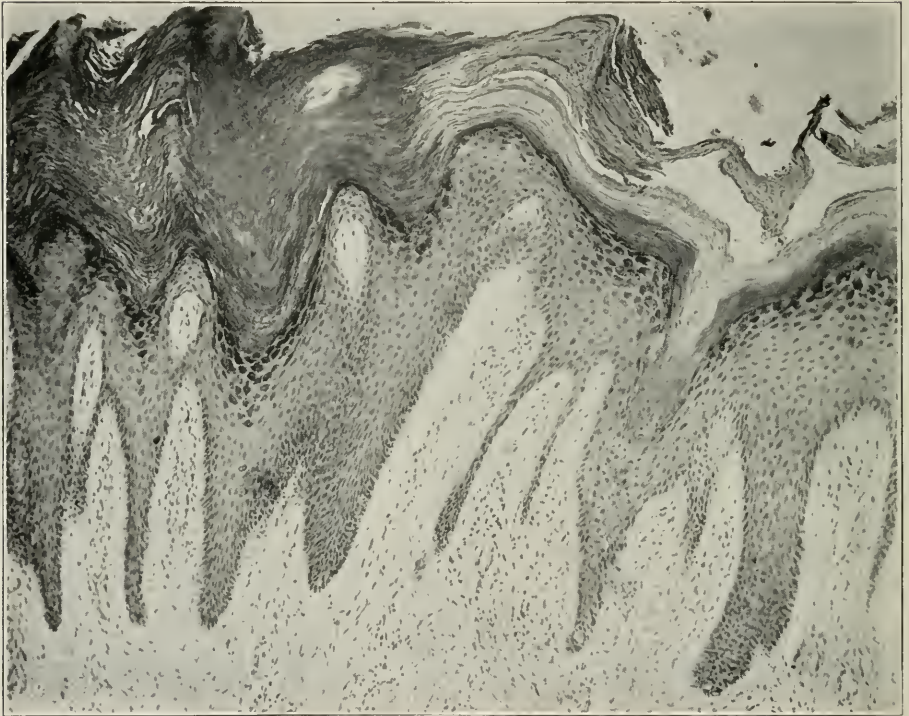


Fig. 9.—Peripheral wall, showing crater and plug in sweat duct.

keratosis over the sweat duct openings. Objectively, there was no peripheral wall and no tendency to eccentric growth. Matosumoto recognized this as a peculiar form of porokeratosis and suggested the name "porokeratosis eccentrica." There is little to recommend this

32. Isaac: Porokeratosis Mibelli, Berl. Dermat. Gesellsch., July, 1913; Ref. Derm. Wchnsch., **57**:981.

33. Matosumoto: A Peculiar Form of Porokeratosis, J. Cutan. Dis. **34**:489, 1916.

case as one of porokeratosis Mibelli, the only analogous finding being the keratosis of the sweat ducts.

McCormac and Pellier,³⁴ in 1918, reported a case in a man, aged 27, in whom the disease had started at the age of 25. Typical lesions were found on the tongue, and the writers presented this fact as an argument against the sweat duct origin of the disease. Matosumoto's³⁵ cases, of which he made a brief tabulated report, were more likely cases of linear nevus. Both clinically and histologically they corresponded more closely with the latter disease than with porokeratosis. In all of his cases he found follicular keratosis, and he maintained that the follicles were implicated to the same extent as the sweat ducts. As he was not dealing with a true Mibelli's disease, his observations are of little value. A considerable number of reports from the Japanese literature are included in Matosumoto's bibliography. These cases are unavailable for this study.

Sevenig,³⁶ in November, 1918, reported a case and discussed the classification of the disease.

In 1914, Sellei³⁷ reported the case of a man, aged 45 years, who had had the condition since the age of 8. Each year the nails of the toes had dropped off. There were many lesions on the palms and soles.

In April, 1920, Bruck and Hirsch³⁸ saw a case, examined it clinically and histologically and decided that porokeratosis belonged in the group of nevi. Their report gives a comprehensive review of the literature.

ETIOLOGY

In spite of the numerous theories which have been advanced as to the etiology of this affection and the experimental work that has been directed toward that end, it must still be regarded as entirely unknown. The part that heredity plays cannot be denied. It was first suggested by two of the cases of Mibelli, in which a brother and sister were affected; and was later strikingly illustrated by Gilchrist, who found eleven members in one family with the disease, and Pasini, who saw twenty-six cases in one family. Many other writers have made the same observation, although occasionally a case has been reported in

34. McCormac and Pellier: A Case of Porokeratosis, *Brit. J. Dermat.* Oct.-Dec., 1918, p. 197.

35. Matosumoto: The So-called Porokeratosis (Mibelli), with Special Reference to Its Histopathology, *J. Cutan. Dis.*, July, 1918, p. 379.

36. Sevenig: Ein Beitrag zum Frage der Porokeratosis Mibelli, *Dermat. Ztsch.*, November, 1918, p. 292.

37. Sellei: Ein Fall von Porokeratosis, *Dermat. Wehnschr.*, April, 1919, p. 241.

38. Bruck and Hirsch: Ueber Porokeratosis Mibelli, *Dermat. Ztschr.*, April, 1920, p. 221.

which the family history was entirely negative. The part that heredity plays is well illustrated in our case. The description of the lesions present in the grandmother and father, as set forth by the patient, leaves little doubt that they were typically those of porokeratosis. The daughter was examined personally, and a typical early lesion was found on the left knee. The crater around the border of the lesion was indistinctly visible. The lesion was apruritic.

The original theory of Mibelli was that the lesions came under the classification of nevi, and that they resulted from some congenital cell rests in the skin. Even as late as 1905 he still clung to this belief. Truffi held that the development of the lesions for the first time in a person of 55 disproved such a theory. Lombardo³⁹ has recorded a brief report of an example of porokeratosis with carcinoma developing in one of the lesions. It is well known that carcinoma frequently develops in nevi, and, according to the theory of Cohnheim, carcinoma is supposed to originate from cell rests. Thus we might argue that the lesions of porokeratosis develop from cell rests, but the analogy is only suggestive. Most recent writers, among them Bruck and Hirsch, favor the nevus theory.

Respighi, in spite of negative experimental work, favored a parasitic theory. Other writers, including Basch and Wende, have attempted to find a parasite, but except for Wende's one successful inoculation into his original patient, all trials have been without results. The success of Wile and Kingery in reproducing molluscum contagiosum and verruca with material ground up and passed through a Berkefeld filter suggested the idea of attempting similar experiments with porokeratosis, and in spite of the unsuccessful attempts of other workers to reproduce the disease, the experiment was carried out. No lesions have ever appeared at the sites of injection. There is nothing to recommend a contagious theory for this disease and much against it. In no case has the wife of a patient having porokeratosis been affected with the disease or vice versa. All attempts at inoculation have been negative; all attempts to grow an organism on various mediums have been without results; and special stains have shown nothing.

In Truffi's case the distribution would suggest probably a neurogenous origin. Each group of lesions was mapped out according to the distribution of a peripheral nerve. This theory was suggested by Respighi in his original article, but denied in the same breath. Other cases, such as Pavlow's, Baum's and Maki's, have favored this suggestion.

39. Lombardo: Auf dem Boden einer Porokeratose entwickelndes Epitheliom, Abstr. in *Monatsh. f. prakt. Dermat.*, April, 1908; *Gior. ital. d. mal. ven.* 6: 1907.

AGE INCIDENCE

In twelve of thirty cases in which the age at which the first lesion appeared was stated, it began before the age of 10, in eight before 20, in four before 30, and the remaining eight from 30 to 35. From this it may be seen that the affection may begin at any age, but more commonly in the earlier years of life. Our patient had had lesions since infancy, and the father's were present throughout his entire life. The affected daughter at present is 9 and has had the lesion on her leg since infancy.

DISTRIBUTION

There is a distinct predilection for the hands and feet, genitals buttocks and scalp, although it may appear at any site. The percentage of cases in which lesions of the mucous membrane occur is high, though not exactly known, for in some instances they were unrecognized and occasionally were not looked for. The palms and soles are almost invariably free; one or two exceptions to this have been recorded.

PATHOGENESIS

Mibelli, in his first work, laid stress on the constant involvement of the sweat ducts and believed that the disease had its origin in the mouths of the ducts. Respighi, in his simultaneous publication, held that the sweat duct orifices and the follicles shared equally in the process, and that either might be the point of origin. The general histologic picture described by the two authors was almost identical. Subsequent writers agreed on an epidermic origin, either in the sweat ducts or in both the ducts and follicles, until 1898, when Respighi and Ducrey suggested a dermic origin.

The histologic study of many sections from our case shows the follicles and orifices of the sebaceous glands to be as constantly involved and in the same way as the sweat duct orifices. However, it does not seem that one can definitely state that the disease has its origin in these structures. The earliest sections show an acanthosis and a considerable degree of cellular infiltration in the cutis. The hyperkeratosis at this stage is slight and the least striking feature of the microscopic picture. For this reason it would be more justifiable to assume that the origin is either in the thickened prickle cell layer or in the papillary layer of the corium. It is true that the early acanthosis is almost immediately followed by a parakeratosis and plugs reaching down into the follicles and gland orifices, but this feature is no more striking than in many other conditions, as Heidingsfeld's studies showed.

There is other evidence to suggest that the origin is not in the sweat ducts. First, the presence of lesions on the mucous membranes is in every way typical, and they correspond closely to those occurring

on the skin. Second, against such an origin and favoring an origin deeper in the skin is the fact that curettement of the lesions is followed by recurrence, while total excision results in cure.

TREATMENT

In his final case report, Mibelli classified porokeratosis among the incurable dermatoses. The results of other writers in treating the condition would tend to support this view. Complete excision has been found to be successful for individual lesions, as has also carbon dioxid, but both of these methods are impracticable in cases in which the patches cover large areas. Following our patient's entrance into this hospital, the roentgen ray was at once applied to all the lesions, a suberythema dose being used. This dosage was repeated every two weeks until five successive treatments had been given. Other than a slight lessening of the pruritus, there was no change in the condition, which was surprising, considering the rapid involution of verruca and other hyperkeratotic and parakeratotic conditions under the ray. Excision and cautery were then tried and so far have been followed by no recurrence. The extent and localization of the eruption preclude the extensive use of either of these methods in our case.

CLASSIFICATION

Throughout the literature of porokeratosis there has been a great diversity of opinion as to its classification. From a résumé of its clinical and histologic characteristics, it would seem that it might best be placed among the verrucae or the nevi. In favor of the former is the wartlike appearance of the lesions, particularly in the earlier stages. Histologically, the epidermal and papillary hypertrophy and the marked hyperkeratonization correspond to the picture of verrucae. The familial tendency, the persistence of the lesions throughout life, the absence of inflammatory changes, the noncontagiousness, the occasional systematic arrangement and the failure to respond to the roentgen ray speak strongly in favor of the placing of porokeratosis among the nevi. Until the etiology and the point of origin of the lesions are understood, a definite classification is impossible. At the present time it is generally included among the hypertrophies of the skin without any attempt at a more definite grouping. From our study it would seem better placed among the verrucous nevi.

CONCLUSIONS

1. Porokeratosis is a distinct clinical entity characterized by a familial tendency and a characteristic clinical and histologic picture.

2. Clinically it is characterized by the occurrence of elevated, wart-like lesions which, as they enlarge, form an irregular peripheral wall surrounding an atrophic depressed center.

3. Histologically it is characterized first by an acanthosis and by inflammatory changes in the corium, which are rapidly followed by a hyperkeratosis with plugging of the sweat ducts and follicles.

4. Porokeratosis is best classified under the group of verrucous nevi because of the wartlike character of the lesions clinically, the epidermal hypertrophy as observed histologically, the familial tendency, the noncontagiousness, the persistence throughout life, the absence of inflammatory changes, the occasional systematic arrangement and the failure to involute under the ray.

ABSTRACT OF DISCUSSION

DR. AUGUST RAVOGLI, Cincinnati: I have always considered porokeratosis to be nothing less than a very limited form of lichen. The slight itching sensation and the formation of the small papules which remain for a long time, sometimes for six months or a year, without change, neither increasing nor diminishing, is in favor of this resemblance. The pathologic specimen which Dr. Wright presented looks a great deal like the condition found in pityriasis rubra pilaris, in which there is a slight infiltration in the derma and an increased quantity of epidermis all around the hair follicles and glands. For this reason I have always regarded this disorder to be nothing less than an attenuated and circumscribed condition, probably identical with lichen planus.

DR. FRED WISE, New York: I have never seen a case. I was particularly pleased with Dr. Wright's classification of the disease as a nevus because those who have studied the disease, taking into consideration the structure, class it as a form of nevus, such as von Recklinghausen's disease and keratosis plantaris and palmaris, and so on. One point that has interested me in looking over the literature of the subject is an article in a Japanese journal in which the author classifies several cases as porokeratosis—cases which I and others to whom I showed the article regard as ordinary linear nevus. In these examples he did not describe any central involution so far as I could ascertain. It is a question in my mind whether those two conditions should be correlated, although we admit that they are both nevi. Porokeratosis and linear nevus should not be classed together. The name porokeratosis should be limited to the lesions with a depressed center and raised acanthotic peripheral wall.

DR. CARROLL S. WRIGHT, Ann Arbor, Mich.: In regard to Dr. Ravogli's suggestion that the disease resembles lichen planus: In going through the literature I found many other cases reported as porokeratosis which on careful study were found to be true cases of lichen planus. However, in our case there were no lesions suggestive of lichen planus, either clinically or pathologically. As to the histologic picture resembling pityriasis rubra pilaris, it is true that it is a disease of the sweat ducts and hair follicles, but this is the only point of resemblance. Heidingsfeld in 1916 made a complete examination of the diseases which he found associated with the sweat ducts and hair follicles. Among these were pityriasis rubra pilaris, porokeratosis and some others. We also reviewed the cases to which Dr. Wise has called attention and thought that they were cases of linear nevus. In no case was there present the central involution which characterizes the late stages of the disease. There was only a slight resemblance to the cases seen in these instances. They are the cases reported by Matsumoto.

XXIV.—IMMUNITY STUDIES IN EXPERIMENTAL SYPHILIS *

II. SPIROCHETICIDAL PROPERTIES OF SERUMS IN LATENT AND EXPERIMENTAL SYPHILIS WITH SOME OBSERVATIONS ON IMMUNITY

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INTRODUCTION

The vast amount of literature dealing with the problem of immunity in syphilis may be grouped into a series of extensive clinical observations, on the one hand, and on the other, the report of a considerable amount of experimental work which received its first impulse from the pioneer studies on syphilis transmission in chimpanzees by Metchnikoff and Roux¹ two years prior to Schaudinn's discovery of *Spirochaeta pallida*. The conclusions, which were drawn from both the clinical and experimental data that had accumulated during a period of years, were, in the first instance, the result of observations not subject to control, and, with the causative agent yet unknown, could not be interpreted scientifically; in the second instance, the experimental findings, without exception, were based on what is now known to be an erroneous conception of the nature and behavior of the syphilitic virus within the animal body.

Reinoculation in Syphilis.—From the clinical studies of Levaditi,² Neisser,³ Finger and Landsteiner⁴ and others, we reach the conclusions that in the syphilitic patient definite resistance to reinoculation is acquired shortly after the appearance of the primary lesion; that the resistance is manifest throughout the secondary stage and in the tertiary stage in which, however, reinoculation becomes more frequently possible, after a certain time; that susceptibility to reinfection may

*Work done under a partial grant from the U. S. Interdepartmental Social Hygiene Board, Washington, D. C.

* Studies, reports and observations from the dermatological department of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Metchnikoff and Roux: Ann. de l'inst. Pasteur **17**:809, 1903; **18**:1, 659, 1904; **19**:673, 1905; **20**:875, 1906.

2. Levaditi: Ztschr. f. Immunitätsforsch., 1910, Ref., Pt. 2, p. 277.

3. Neisser: Beiträge zur Pathologie und Therapie der Syphilis, Berlin, Julius Springer, 1911.

4. Finger and Landsteiner: Arch. f. Dermat. u. Syph. **78**:335, 1906; **81**: No. 1, 1906.

return even though the syphilis has been entirely cured, although in this regard a difference in degree of susceptibility prevails as compared with the susceptibility of a normal person.

Animal experimentation has led to definite conclusions which are correlated in the main with the earlier clinical observations and indicate a state within the animal body comparable with ideas of immunity expressed in the foregoing, in which progressively increasing resistance is developed as the syphilitic virus becomes generally distributed, until during the early tertiary stage this resistance reaches a maximum. In reviewing the work done by different investigators, we find two distinct points of view expressed. Neisser, for instance, is representative of those who believe that no immunity to syphilis exists, and that failure to reinoculate means an existing syphilis rather than any definite immune condition. In support of this theory he has adduced a number of positive inoculations with emulsions of bone marrow and spleen from monkeys which had resisted a second infection. On the other hand, animals which had been cured by drugs could be reinoculated. Finger and Landsteiner⁵ have taken a different view, and much of the later experimental work in syphilis is in accord with their idea that immunity increases gradually with the onset of the disease and becomes absolute during the "second latent period" preceding the tertiary stage when gummatous lesions may be developed. It is to be noted, in this place, that the interpretation of "immunity" phenomena has rested primarily on the principle of resistance which is developed in the host after the syphilitic virus has become generally distributed. This idea, although reasonably consistent with ordinary immunity phenomena, was based, however, on inadequate knowledge.

Localized Reactions and Tissue Immunity.—Early investigations by Metchnikoff, Roux, and Neisser had brought out the fact that experimental syphilis in monkeys gave rise to immune properties of the skin similar to that found in man; that is, reinfections were not possible at a time when a primary lesion was manifest. In confirming these observations an attempt was made by Kraus and Volk⁶ to explain the paradoxical reaction in persons with generalized syphilis in whom cutaneous infections could rarely, if ever, be elicited by reinoculation. It appeared that resistance developed slowly and was at its height only after a long time. Superinfections were possible up to about three weeks after the first inoculation and prior to the appearance of a primary lesion. Reinfection failed, as a rule, after the lesion had persisted for several days. Under these conditions superinfections were characterized by

5. Finger and Landsteiner: Verhandl. d. deutsch. Dermat. Gesellsch., IX Kongress, Springer, 1907, p. 25.

6. Kraus and Volk: Wien. klin. Wchnschr. **19**:621, 1906.

their relatively benign appearance and much smaller size as compared with the ordinary initial lesion. That the size and type of lesions may be influenced by preexisting ones has been mentioned by Nichols,⁷ and Brown and Pearce⁸ in later studies. The possible influence of primary foci on the subsequent development of later lesions had already been suspected by Kraus and Volk,⁶ and in a few of their experiments rudimentary manifestations were observed when lesions were excised from seven to fourteen days after their appearance. From this it was concluded that a skin immunity appeared to prevail in the same degree as before and that a partial immunity seemed to develop as a result of inoculation of the surface of the skin. An explanation of the previously described phenomenon of resistance to reinfection by way of the skin and mucous membrane at a time when certain organs and tissues continue to undergo injury must be sought for in the behavior of certain tissues, such as the rabbit testicle, for example. It has been found that apparent recovery from a previous lesion develops a resistance to subsequent inoculation, although ordinarily no generalized resistance in rabbits appears to develop during the disease, since the opposite testicle can be successfully inoculated before, during and after the existence of a lesion on the other side. Observations of many investigators point to the probability of a localized reaction existing in the animal body, in consequence of a mechanism by which active invasion with *Spirochaeta pallida* leads to a state of nonsusceptibility. Neisser has called this condition "Anergie." It is conceivable that organisms which may gain entrance at this time may remain uninjured and yet be capable of setting up lesions in other parts of the body. There is evidence from recent studies on the dissemination of *Spirochaeta pallida* and the so-called "carrier state" in latent syphilis that such may be the case. At all events, it seems to be of some importance to differentiate between the classic conception of immunity to syphilis and the state of affairs which is probably more consistent with present-day knowledge of infection with this disease.

Our own investigations in latency in man⁹ and in experimental syphilis, together with the observations of Brown and Pearce,¹⁰ have

7. Nichols, Henry J.: Observations on the Pathology of Syphilis. J. A. M. A. **63**:466 (Aug. 8) 1914.

8. Brown and Pearce: J. Exper. M. **32**:445, 1920.

9. Eberson, F., and Engman, Martin F.: An Experimental Study of the Latent Syphilitic as a Carrier. J. A. M. A. **76**:160 (Jan. 15) 1921. Eberson, F.: Dissemination of *Spirochaeta Pallida* in Experimental Syphilis. Arch. Dermat. & Syph. **3**:111 (Jan.) 1921; XXIII.—Immunity Studies in Experimental Syphilis. Infectivity and Survival of *Spirochaeta Pallida* in Rabbits, with Observations on Some Strains from Latent Syphilis. Ibid. **3**:775 (June) 1921.

10. Brown, W. H., and Pearce, L.: Note on Dissemination of *Spirochaeta Pallida* from Primary Focus of Infection. Arch. Dermat. & Syph. **2**:470 (Oct.) 1920.

established the significance of the lymphatic glands as foci from which *Spirochaeta pallida* may be discharged. The rôle which this type of localization may play in immunity may be conjectured. It is not mere speculation to attribute an immunity response to the presence of these organisms since we know that resistance to reinoculation is associated with the presence of spirochetes in some part of the body. Foci in which "latent" spirochetes are localized may act as centers from which antibodies are slowly elaborated and then discharged into the blood stream. From a consideration of an extreme type of localization, such as that found in glands, we next pass on to a study of the immunity phenomena which may be seen to occur in single lesions.

Local Lesions and Inhibitory Effects on Development of Lesions Elsewhere.—Some of the early experiments made with monkeys demonstrated the inhibitory effect exercised by lesions in one organ on the development of lesions in other parts of the body (Metchnikoff and Roux). Using the rabbit testicle for his study, Nichols⁷ found that unilateral inoculation when followed by castration of the infected testicle promptly gave rise to lesions in the opposite testicle. The fundamental importance of these observations has led to intensive study of the cyclic changes in syphilis and to those factors which tend to shed much light on immunity reactions in the experimental animal. From the standpoint of immunity response to infection it would be of great value to interpret types of lesions as evidence of a certain kind of reaction, although the change in the character of lesions makes such interpretation difficult. There is evidence, however, that resistance of the animal to *Spirochaeta pallida* is intimately connected with the nature and extent of the reaction taking place at the site of inoculation, and any influence which is capable of modifying the reaction might be expected, according to Brown and Pearce,¹¹ to react on the phenomena of the infection as a whole. In their opinion, generalization is the measure of resistance. The protection which is developed from any given focus may not affect all tissues or all parts of the body to the same degree, but it may be extended progressively from primary lesions to the successive groups of tissues and manifest protective action in one group at a time when other groups of tissues may be afforded little or no protection. The fact that tissue immunity may manifest itself by extension from group to group has direct bearing on the view which we have expressed regarding the elaboration of antibodies by way of localized areas into the blood stream.

11. Brown, W. H., and Pearce, L.: Experimental Production of Clinical Types of Syphilis in the Rabbit, *Arch. Dermat. & Syph.* **3**:254 (March) 1921.

Cyclic Reactions in Syphilis and Analogous Phenomena of Trypanosome and Spirillary Diseases.—Cyclic phenomena in syphilis find a counterpart in other diseases which are caused by spirochetes. In relapsing fever the periodic functioning of a protective mechanism is known to take place in the blood of infected individuals, or as Levaditi¹² believes, to manifest itself as a phagocytic reaction which is independent of serum properties. African tick fever offers analogous phenomena, and although recurrences are more common, susceptible animals are immune for a period following a second attack. A similar immunity follows recovery from spironematosis in geese and other fowls. The mechanism on which such immunity depends has been studied by numerous investigators, notably by Gabritschewsky,¹³ Marchoux and Salimbeni,¹⁴ Levaditi,¹² Levaditi and Manouelian,¹⁵ Mesnil and Nicolle,¹⁶ Neufeld and von Prowazek,¹⁷ and others. To Gabritschewsky we owe our knowledge of the bactericidal content of blood in relapsing fever in which the protective property was found to be at a maximum after the crisis, diminished during apyrexia and increased again during the next attack. Notwithstanding these fluctuations, immunity as a whole increased in the course of the disease. The protection afforded by active immunity in these different diseases is not wholly dependent on bactericidal properties in the serum, for as Novy and Knapp¹⁸ have pointed out, other immune bodies may play an important part in the mechanism of defense. More recently Inada and his collaborators¹⁹ demonstrated in the blood serum of patients with Weil's disease the presence of a specific lysin for the spironema. Immune bodies may be present four years or more after the attack of disease.

In diseases caused by trypanosomes the facts are similar to those given in regard to spirochete infections. The attributes common to all of these seem to be a resistance to reinfection which coexists with the presence of the living organisms in the host. Syphilis in this respect is analogous in its behavior, not only from the standpoints which have been discussed, but also in regard to certain localizing characteristics of *Spirochaeta pallida* and the reactions attending their dissemination.

12. Levaditi: Compt. rend. Soc. de Biol. **60**:134, 1906; Ann. de l'inst. Pasteur **20**:41, 1906.

13. Gabritschewsky: Ann. de l'inst. Pasteur **10**:629, 1896.

14. Marchoux and Salimbeni: Ann. de l'inst. Pasteur **17**:569, 1903.

15. Levaditi and Manouelian: Ann. de l'inst. Pasteur **20**:593, 1906.

16. Mesnil and Nicolle: Ann. de l'inst. Pasteur **20**:513, 1906.

17. Neufeld and von Prowazek: Centralbl. f. Bakteriöl. Ref., Abt. 1 **41**:754, 1908.

18. Novy and Knapp: J. Infect. Dis. **3**:291, 1906.

19. Inada, Ido et al: J. Exper. M. **33**:377, 1916.

Analogies may be found again, for example, in diseases of fowls in which *Spirochaeta gallinarum* has been shown to localize in certain viscera and to enter the blood stream by way of diverse glandular tissues.¹⁵

In weighing the analogy of syphilis to other diseases, one must not lose sight of the fact that the ordinary conception of immunity defines a condition which is the result of a refractory state incompatible with the existence of the organism causing the disease. From the biologic point of view, the cycle in syphilis would tend to disprove the theory that immunity is not possible at any stage of the infection.

EXPERIMENTAL IMMUNITY IN SYPHILIS

Antibody Phenomena.—Serologic studies in experimental syphilis have been concerned mainly with the development in serums of agglutinating and complement-fixing bodies. Attempts to demonstrate specific agglutinins in human and experimental syphilis were made by Hoffmann,²⁰ Landsteiner and Mucha,²¹ Hoffmann and von Prowazek,²² Uhlenhuth and Mulzer,²³ Metchnikoff and Roux,¹ and others, with negative or indecisive results. Following Noguchi's discovery, in 1911, of a method for isolating *Spirochaeta pallida* in pure culture, he was able to demonstrate in immunized rabbits the presence of agglutinins and complement-fixing substances for cultivated strains. The first successful experiments were reported by Kolmer²⁴ and were followed soon afterward by those of Nakano²⁵ and Kissmeyer.²⁶ With pure cultures of the spirochetes it was possible to develop highly agglutinating serums from rabbits. Serums from individuals in the primary, secondary and tertiary stage and from congenital syphilis were found to contain agglutinins in about 50 per cent. of the cases. These antibodies were shown to be present in highest concentration during the later stages of the disease and in the greatest percentage of cases among persons who showed late primary, secondary, tertiary and latent syphilis (Kolmer, Broadwell and Matsunami²⁷). That the reactions of culture *Spirochaeta pallida* differed from those which were obtained from human lesions was next shown by Zinsser, Hopkins and McBurney.²⁸

20. Hoffmann: Dermat. Ztschr. **13**:561, 1906.

21. Landsteiner and Mucha: Centralbl. f. Bakteriöl., Ref. **39**:540, 1907.

22. Hoffmann and von Prowazek: Arb. a. d. k. Gsndhtsamte **37**:205, 1911.

23. Uhlenhuth and Mulzer: Arb. a. d. k. Gsndhtsamte **33**:183, 1909.

24. Kolmer: J. Exper. M. **18**:18, 1913.

25. Nakano: Arch. f. Dermat. u. Syph. **116**:265, 1913.

26. Kissmeyer: Deutsch. med. Wchnschr. **41**:306, 1915.

27. Kolmer, Broadwell and Matsunami: J. Exper. M. **24**:333, 1916.

28. Zinsser, Hopkins and McBurney: J. Exper. M. **23**:341, 1916.

in a study of agglutinins in serums from animals immunized with culture spirochetes.

Protective Properties of Serum in Human and Experimental Syphilis.—Few references are found in the literature pertaining to protection experiments made in vitro and in vivo with serums from persons or infected animals. Metchnikoff and Roux found serums from monkeys which had been systematically treated with attenuated syphilitic virus ineffective in preventing animal infection with material obtained from active lesions. They believed, however, that they had demonstrated in two instances a definite protective antibody in serum from a monkey which had received subcutaneous injections with syphilitic blood for a period of eight months. A chimpanzee that had been inoculated with a mixture of such serum and material from a chancre remained negative for thirty-eight days, when death from pneumonia supervened. Another monkey, inoculated similarly, evidenced slight lesions as compared with a control. These results appear to be indecisive. Two therapeutic experiments with serums from infected monkeys, reported by Finger and Landsteiner, cannot be interpreted owing to the technic employed. Local subcutaneous injections of serum in a total amount of 59 c.c. failed to prevent roseola which developed eight weeks after primary genital lesions. In both patients the primary lesions were excised previous to administration of the serum. The generalization which follows as a result of extirpation of the primary foci would tend to mask the result of these therapeutic measures.

Spirocheticidal activity of serums has been studied in rare instances. Finger and Landsteiner²⁹ reported negative results with serums from florid stages of syphilis. In vitro experiments, described by Zinsser and Hopkins,²⁹ demonstrated spirocheticidal properties for culture strains in the serum of rabbits and sheep that had been immunized with cultures of *Spirochaeta pallida*. With virulent spirochetes obtained directly from lesions, this protective property was not manifested by serum produced with culture spirochetes.²⁸ These results were confirmed by Noguchi,³⁰ who found, in addition, that serum from a syphilitic rabbit destroyed culture spirochetes.

EXPERIMENTAL

The experiments which are reported in this paper have been based on the idea that syphilis may offer immunity phenomena analogous or similar to those that are found in other infections which tend to assume a latent or carrier state. In order that the nature of a protective mechanism might be studied more effectively and be subject to control,

29. Zinsser and Hopkins: J. Exper. M. **23**:323, 1916.

30. Noguchi: J. Exper. M. **25**:765, 1917.

the method of experimental infection was designed so as to permit a study of serum properties at different stages of the disease. These animal experiments were planned to supplement the data which might be obtained from an investigation of serums taken from persons having latent syphilis. The protective property of specimens of serums was measured by the presence or absence of spirocheticidal activity when combined with living, virulent *Spirochaetae pallidae* derived from active syphilitic lesions in rabbits. It is recognized that there is great difficulty in determining an effective combination of dosage of spirochetes, volume of serums, time of incubation and the amount of the mixture to be injected finally as a test of antibody content. Since no attempt was made to minimize the chances of infecting the experimental animal, this should be borne in mind when weighing the negative results in which the given stage of infection might have a direct bearing on the protective property of such serum as was used in the test. Detailed quantitative procedures that would measure different degrees of spirocheticidal activity against diminishing doses of virulent organisms could not be followed owing to lack of space and material. The numerous control experiments in which normal serums were used against fixed doses of spirochetes in a manner comparable with the test serums in all particulars were the criteria in every series.

Material and Scope of Experiments.—A study was made of the spirocheticidal property of different serums from patients known to have latent syphilis with a history of old as well as more recent infection, and from experimentally infected rabbits. In the group of animal experiments a considerable amount of material was available for the study of protective serum properties during the various stages of syphilitic infection. The patients who were selected for study were free from visible syphilitic manifestations or symptoms and were for the most part untreated cases.

Technic.—Blood from patients was drawn with sterile precautions by means of a glass syringe from the median vein of the arm. Specimens were allowed to stand at room temperature until the clot was formed and then kept in the ice chest for one half hour before centrifugation. The clear serum was next heated at 54 C. for twenty minutes and stored in hermetically sealed tubes until needed. Serum was from one to four weeks old and never exceeded six weeks at the time experiments were made. Experimentally infected rabbits were bled from the heart, under ether anesthesia, and the serum treated similarly to that which was obtained from patients. Rabbit serums were from two to five weeks old at the time tests were made.

A combined in vitro and in vivo method was used in determining the spirocheticidal activity of serums which were combined in amounts

of 2 c.c. with 0.1 c.c. of a suspension of virulent *Spirochaeta pallida*. The mixtures were incubated in a water bath at 37 C. for one and one half hours and then injected intratesticularly into normal rabbits, in duplicate series for each strain of spirochetes which were used in the test. Normal human and normal rabbit serums served as controls and were subjected to every step in the technic in parallel with the test serums.

Animals Used.—Medium-sized gray and brown rabbits with well developed testicles were used. At the time of inoculation the animals were from 5 to 6 months old, as a rule.

Strains of Spirochaeta Pallida Used.—Three strains of *Spirochaeta pallida* were isolated originally from a penile chancre (No. 170), the gland of a patient with latent syphilis (No. 137) and from the semen of a patient with latent syphilis (No. 117), respectively. Spirochetolytic properties of serums from the latent cases were studied against at least two strains and in some instances with three. Of these strains, No. 170 was used constantly along with either the latent strain No. 137 or No. 117. In this place mention may be made of the fact that no difference in the protective property of the serum was found to exist for any special organism. When definite spirocheticidal activity was present, all of the strains failed to infect, irrespective of their origin. This was not the general rule, however, with serums that were taken from experimentally inoculated rabbits, as will be shown later. Emulsions of *Spirochaeta pallida* were prepared from testicular lesions in rabbits with active syphilis. The strains were transferred from animal to animal at stated intervals and were uniformly and constantly virulent. A small amount of material was taken directly from the lesion by means of a finely drawn out capillary glass pipet. Warm salt solution was added in a small volume to the testicular puncture fluid which was expelled into a sterile Petri dish with the aid of a rubber nipple attached to the pipet. A sterile glass rod, flattened at one end and bent at a convenient angle, was used to grind up the sticky mass in the smallest possible volume of solution. This was next drawn up into a pipet through a thin layer of sterile absorbent cotton placed in the homogenous emulsion. The perfectly clear fluid containing the organisms free from any tissue or foreign material was finally added to the serum and the protective property next studied. Suspensions of this material averaged from 15 to 20 spirochetes per microscopic field.

The rabbits were examined daily after two weeks had elapsed. The testicles of animals that remained negative for two months or longer were punctured at different intervals and dark-field examinations made of the testicular fluid over a period of six months. In a number of instances such animals were anesthetized and the emulsions of testicle,

liver and spleen, and in some cases the inguinal glands were injected into a series of normal rabbits to ascertain the fate of *Spirochaeta pallida* which were introduced with the serums. At no time were these subinoculations into the testicle successful, showing that those animals were negative which failed to develop lesions synchronously with or approximately at the time the control animals were found positive.

RESULTS OF EXPERIMENTS WITH HUMAN SERUMS

Eighteen specimens of blood serum from persons having latent syphilis were found to have spirocheticidal properties for different strains of *Spirochaeta pallida*. In those cases in which true latency did not exist, no protection was manifested by the serum. A history of recent infection invariably confirmed the experimental results in these instances.

TABLE 1.—RESULTS IN EXPERIMENT 1.

Serum	Spirochete		Strain of S. pallida	Result
	Amount c.c.	Suspension c.c.		
H. Mc. D.....	2.0	0.1	170, 137	Negative; animals remained well
W. M.....	2.0	0.1	170, 137, 117	Negative; animals remained well
H. A.....	2.0	0.1	170, 117	Negative; animals remained well
H. B.....	2.0	0.1	170, 137	Negative; animals remained well
J. A.....	2.0	0.1	170, 137	Negative; animals remained well
C. B.....	2.0	0.1	170, 117	Negative; animals remained well
Normal human..	2.0	0.1	170, 137, 117	Positive lesions after 28, 34, 36 days
Normal rabbit...	2.0	0.1	169, 170 137, 117	Positive lesions after from 4 to 5 weeks, on the average

In Experiment 1 are tabulated the results which were obtained with serums from persons whose infection dated back from three to twenty-five years. The blood Wassermann reactions in these and succeeding protocols refer to specimens which were taken just prior to the experiment, unless specified otherwise.

Clinical Data.—M. Mc. D., a man, aged 55, gave a history of a primary lesion twenty years ago. The history as to antisyphilitic treatment was vague. His wife had had one stillbirth. The blood Wassermann reaction was + + + +.

W. M., a man, aged 45, gave a history of a penile chancre twenty-five years ago. The blood Wassermann reaction was + + + + in the cholesterin antigen. There was clinical evidence of hepatic cirrhosis.

H. A., a man, aged 32, had had a chancre eight or nine years ago, with secondary eruption at the time. The blood Wassermann reaction was + + + +.

H. B., a man, aged 29, gave a history of a chancre on the penis five years ago. His wife had had no miscarriages. The blood Wassermann reaction was + + + +.

J. A., a man, aged 26, had had a chancre four or five years ago, with no eruption at the time. The blood Wassermann reaction was + + + + in the cholesterin antigen and + in the noncholesterin antigen.

C. B., a man, aged 31, gave a history of a chancre three years ago. There was no eruption at the time. His wife had had no miscarriages. The blood Wassermann reaction was + + + + in the cholesterin antigen and + + in the noncholesterin antigen.

The next experiment illustrates the spirocheticidal activity in serum from a patient who had received antisyphilitic treatment until the Wassermann reaction was persistently negative. Another interesting observation brought out in this series is that spirocheticidal bodies may be present in the serum of an infant in common with those present in the mother's serum.

Clinical Data.—M. W., a woman, aged 45, had been taking antisyphilitic treatment for an indefinite period up to about fourteen months prior to the time her serum was obtained for the experiment. Her blood Wassermann reactions were successively negative at intervals of six months and she was classified as "serologically well."

TABLE 2.—RESULTS IN EXPERIMENT 2.

Serum	Spirochete			Result
	Amount c.c.	Suspension c.c.	Strain of <i>S. pallida</i>	
M. W.....	2.0	0.1	170, 137	Negative; animals remained well
M. L. D.....	2.0	0.1	170, 137	Negative; animals remained well
D. L. D.....	2.0	0.1	170, 137	Negative; animals remained well
Normal rabbitN.	2.0	0.1	170, 137, 117	Positive lesions after 4 to 7 weeks
Normal human..	2.0	0.1	170, 137, 117, 169	Positive lesions after 4 to 7 weeks

M. L. D., a woman, aged 34, gave no history of infection and had received no treatment. Her blood Wassermann reaction was + + + + in the noncholesterin antigen.

D. L. D., a girl, aged 18 months, whose mother is M. L. D., gave a + + + + Wassermann reaction in the noncholesterin antigen only. She was apparently healthy and free from syphilis.

Typical cases of latent syphilis are those in which the patient has no history of an infection, no history of treatment for syphilis at any time, and in which there are no signs or manifestations of the disease. Such persons usually find their way to the clinic for syphilis by way of other clinics to which they may have come for examination. These patients, as a rule, give a positive blood Wassermann reaction in one antigen only, generally the cholesterin antigen. The following experiment which was performed with such a group of patients gave uniform results for spirocheticidal properties in the serums tested.

Clinical Data.—R. C., a woman, aged 31, gave no history of infection, and the patient had never taken any treatment. The blood Wassermann reaction was + + + + in the noncholesterin antigen only.

R. O'N., a woman, aged 33, gave no history of infection. She had had two miscarriages. The blood Wassermann reaction was + + + + in the cholesterin antigen only.

G. B., a woman, aged 33, gave no history of infection or treatment. The blood Wassermann reaction was + + + + in the cholesterin antigen only.

A. S., a woman, aged 27, gave no history of infection or treatment. The blood Wassermann reaction was + + + + in the cholesterin antigen only.

TABLE 3.—RESULTS IN EXPERIMENT 3.

Serum	Spirochete		Strain of <i>S. pallida</i>	Result
	Amount c.c.	Suspension c.c.		
R. C.....	2.0	0.1	170, 137, 117	Negative; animals remained well
R. O'N.....	1.5	0.1	170, 137	Negative; animals remained well
G. B.....	1.5	0.1	170, 117	Negative; animals remained well
A. S.....	2.0	0.1	170, 117	Negative; animals remained well
Normal human..	2.0	0.1	170, 137, 117	Positive lesions after 29, 32 and 35 days, respectively
Normal rabbit...	2.0	0.1	170, 137, 117	Positive lesions after 30, 28 and 30 days, respectively

In Experiment 4 are summarized the results of protection tests for another group of patients who gave no history of infection and whose blood Wassermann reactions were positive in both antigens, or, as in the majority of cases, slightly positive in either one or the other in inverse relationship.

TABLE 4.—RESULTS IN EXPERIMENT 4.

Serum	Spirochete		Strain of <i>S. pallida</i>	Result
	Amount c.c.	Suspension c.c.		
S. S.....	2.0	0.1	170, 137	Negative; animals remained well
J. S.....	2.0	0.1	170, 137	Negative; animals remained well
E. O'N.....	2.0	0.1	170, 137, 117	Negative; animals remained well
L. C.....	2.0	0.1	170, 117	Negative; animals remained well
S. W.....	2.0	0.1	170, 137, 117	Negative; animals remained well
Normal human..	2.0	0.1	170, 137, 117, 169	Positive lesions after 4 to 6 weeks
Normal rabbit...	2.0	0.1	170, 137, 117, 169	Positive lesions after 4 to 6 weeks

Clinical Data.—S. S., a man, aged 28, gave no history of infection. The blood Wassermann reaction was + + + + in the cholesterin antigen and + + in the noncholesterin antigen.

J. S., a woman, gave no history of infection, and her husband's blood Wassermann reaction was negative. The blood Wassermann reaction of the patient was + + + +.

E. O'N., a woman, gave no history of infection or eruption, and there had been no miscarriages. The patient came to the clinic for trigonitis. The blood Wassermann reaction was + + + + in the cholesterin antigen and + in the noncholesterin antigen.

L. C., a woman, gave no history of infection or eruption. She had had one miscarriage. The blood Wassermann reaction was + + + + in the cholesterin antigen and + in the noncholesterin antigen.

S. W., a man, aged 30, gave no history of infection. His wife and only child were well and free from syphilis. The blood Wassermann reaction was + + + + in the cholesterin antigen and + in the noncholesterin antigen.

THE BLOOD SERUM IN EARLY SYPHILIS AND THE LATENT
STAGE OF RECENT INFECTIONS

The presence of a protective property in serums from cases of syphilis would seem to depend on the stage of infection. A difference is to be noted between latency in the sense defined as occurring after a very old infection and the period of latency which occurs early in the disease and as an interval between the possible flaring up of a train of typical symptoms.

The serums from a group of seven patients with histories of recent infection were found uniformly negative for spirocheticidal activity. These results were in marked contrast to those obtained in the other series, and are summarized in Experiment 5.

TABLE 5.—RESULTS IN EXPERIMENT 5.

Serum	Spirochete			Result
	Amount c.c.	Suspen- sion c.c.	Strain of <i>S. pallida</i>	
L. M.....	2.0	0.1	170, 137	Positive lesions after 32 to 38 days
D. W.....	2.0	0.1	170, 137	Positive lesions after 40 to 44 days
J. B.....	2.0	0.1	170, 117	Positive lesions after 48 to 50 days
E. L.....	2.0	0.1	170, 137, 117	Positive lesions after 50 to 52 days
C. W.....	2.0	0.1	170, 117	Positive lesions after 38 to 40 days
F. B.....	2.0	0.1	170, 137	Positive lesions after 55 to 57 days
N. N.....	2.0	0.1	170, 137	Positive lesions after 42 to 44 days
Normal human..	2.0	0.1	170, 137, 117, 169	Positive lesions after 40 to 42 days
Normal rabbit..	2.0	0.1	170, 137, 117, 169	Positive lesions after 36 to 40 days

Clinical Data.—L. M., a woman, aged 32, had had two miscarriages. Her history as to infection was vague. She showed definite signs of active pulmonary tuberculosis. The blood Wassermann reaction was + + + + in both antigens.

D. W., a man, aged 39, gave no history of infection. The blood Wassermann reaction was + + + + in the cholesterin antigen. The patient gave clinical evidence of prostatitis.

J. B., a man, had had a primary lesion on the penis two months ago. The blood Wassermann reaction was + + + + in both antigens.

E. L., a man, aged 30, gave a history of infection eight months ago with a + + + + blood Wassermann reaction at the time. Two months later the reaction was + + + + in the cholesterin antigen. One month afterward, following two weeks of mixed treatment, the reaction was +; a month later it was again + + + +. At the time a specimen of serum was taken for the experiment the Wassermann reaction was negative.

C. W., a man, aged 24, gave a history of a primary sore on the penis two years ago. He had taken three injections of arsphenamin at the time. The blood Wassermann reaction was + + + +.

F. B., a woman, gave no history of infection. She had had two recent miscarriages. Her husband had been taking antisyphilitic treatment. The blood Wassermann reaction was + + + + in the cholesterin antigen and + + in the noncholesterin antigen.

N. N., a woman, gave no history of infection or miscarriages. She had been "feeling ill" for the past two years coincident with her husband's infection which dated back to that time. He had been taking treatment for syphilis during the past year. The patient's Wassermann reaction was + + + + in both antigens.

This series illustrates that there may be a complete correlation between the presence of protective substances in the serum and the stage of the infection. Where true latency has been attained by the individual, the serum exerts a spirocheticidal effect on *Spirochaeta pallida*. On the other hand, where the disease has not yet become latent and where an active focus appears to exist, the serum seems to be devoid of spirocheticidal properties. In one instance an acute infection coexisted with syphilis, so that it is difficult to interpret the result. An intercurrent infection may vitiate the effective functioning of any existing serum properties even in those persons who may be "latent" cases.

PROTECTIVE PROPERTY OF SERUM IN RELATION TO THE WASSERMANN REACTION OF THE BLOOD

No attempt will be made to discuss the matter of antisyphilitic treatment and the measure of its efficiency in terms of the Wassermann reaction, or to evaluate the possible effects which any treatment may have on the natural immunity response to the invading *Spirochaeta pallida*. It is clear from the foregoing experimental study that a negative Wassermann reaction following treatment for syphilis may or may not go hand in hand with spirocheticidal activity of the serum in question. It is equally clear that continued treatment which renders a Wassermann test repeatedly negative does not nullify any protective property which may be present in the serum. The important point is that spirocheticidal activity of serum, irrespective of the Wassermann reaction, is essentially a function of time and depends on the degree to which the individual has elaborated and distributed the slowly accumulating antibodies. A negative blood Wassermann reaction attending treatment of a recent infection is not comparable to a similar result in the case of a person whose infection is of older origin. In the one instance we may find no spirocheticidal serum properties and in the other we may. A temporary negative Wassermann reaction must not be confused with one which is repeatedly negative and in

accordance with which a treated patient may be classified as "serologically well." These points are illustrated in Experiment 2 (M. W.) and in Experiment 5 (E. L. and C. W.).

SPIROCHETICIDAL SERUM AND ITS EFFECT ON THE
DISSEMINATION OF *SPIROCHAETA PALLIDA*

Spirochaetae pallidae are discharged into the blood stream early in the course of infection from a primary focus. The organisms may be recovered from the regional lymph glands or the blood stream as early as forty-eight hours after experimental inoculation and may be present for an indefinite period up to and including the first signs of infection (Brown and Pearce,¹¹ Levaditi¹²).

An experiment was planned with a view to determine the effect of a possible spirocheticidal reaction within the rabbit testicle on the dissemination of *Spirochaeta pallida*. The animals which were used in this group were selected at random from one of the series at a time

TABLE 6.—SUMMARY OF EXPERIMENT 6

Aug. 14, 1920 Series A Rabbit		Sept. 4, 1920 Series B Rabbit
336	2 c.c. blood	353 and 354
337	2 c.c. blood	355 and 356
338	2 c.c. blood	357 and 358
339	2 c.c. blood	359 and 360

when the outcome as to spirocheticidal activity of the serums under test was not known. The results were decisive, although the series was not large.

Experiment 6.—Rabbits were injected intratesticularly with mixtures of serums and virulent *Spirochaeta pallida* to determine the presence of protective substances in the specimens. Twenty-one days later, these animals were bled from the heart under ether anesthesia and 2 c.c. of defibrinated blood injected immediately into the testicles of normal rabbits in duplicate series. The sub-inoculated animals were examined regularly over a period of six months, during which time repeated testicular punctures were made in order to check up the examination. Table 6 is a summary of the experiment.

Results of Inoculation.—Oct. 18, 1920, Rabbit 339 presented a small bean-sized nodule in the testicle. Dark-field examination showed enormous numbers of *Spirochaetae pallidae*. Jan. 6, 1921, rabbits 359 and 360 developed pea-sized nodules in the upper pole of the testicle. Dark-field examination showed enormous numbers of *Spirochaetae pallidae*.

The other animals in both series remained uniformly and persistently negative. When injection with a mixture of spirocheticidal serum and spirochetes resulted in negative inoculations, the blood from these rabbits proved to be free from *Spirochaeta pallida*. When protective action was not manifested by the serum, dissemination occurred in the usual manner. The conclusion, therefore, is that spirocheticidal activity of serum in latent syphilis is of such a character as to prevent the normal dissemination of spirochetes from the primary focus.

THE BLOOD SERUM IN EXPERIMENTALLY INFECTED RABBITS

The rabbit serums which were studied for spirocheticidal properties were obtained from experimentally infected animals at different times after inoculation. Four strains of *Spirochaeta pallida* were used in these experiments. Two were isolated originally from two cases of latent syphilis—from the inguinal gland and semen, respectively—and two were isolated from penile chancres. The strains from latent sources are designated as No. 137 and No. 117, respectively, and the chancre strains as No. 169 and No. 170.

Serums containing suspensions of *Spirochaeta pallida* were injected into a series of normal rabbits in accordance with a combined in vitro and in vivo method which has already been described. Homologous and heterologous strains of spirochetes were used in making spirocheticidal tests. For controls, normal rabbit serums were used and also a number of test serums to which no *Spirochaeta pallida* had been added. The results with the different serums are grouped according to the time after infection when specimens were taken. There is indicated also the number of days which elapsed between the last positive dark-field examination of such infected rabbits and the date when serum was obtained. All subinoculated series of rabbits were kept under observation for from three to four months, during which time repeated testicular punctures and dark-field examinations were made, irrespective of the absence of any lesions.

The experiments are summarized in the following manner: Spirocheticidal activity was developed in the rabbit in the course of from six months to one year after the original infection. During the time that spirochetes were found in lesions and for a certain period during which dark-field examinations yielded persistently negative results, the serum was devoid of protective elements. Strains of *Spirochaeta pallida* from latent sources appeared to develop an immune serum having a wider range of protective action. Whereas such serums exerted spirocheticidal action toward heterologous as well as homologous strains of spirochetes, the serums obtained from rabbits which were inoculated with chancre strains failed to protect against inoculation with heterologous strains, even when the time which had elapsed since infection was comparable to that in the other series of animals (Experiment 3).

Experiment 7.—In this series, the strain of *Spirochaeta pallida* used was isolated from the inguinal gland of a person having latent syphilis (Strain 137). From one to three months after infection, no protective substances were found in the serum. Spirocheticidal substances were found after five months.

TABLE 7.—RESULTS IN EXPERIMENT 7

Serum	Test Strain of <i>S. pallida</i>	Days Positive for <i>S. pallida</i>	Days Negative When Bled	Days Since Infection	Result
(I) 137*	137	26	69	144	Protection; animals well
(II) 137	137	21	40	98	Positive lesions, 42-45 days
(II) 137	(Control)				Negative; animals well
(III) 137	137	14	28	67	Positive lesions after 38 to 42 days
(III) 137	(Control)				Negative; animals remained well
(IV) 137	137	9	10	40	Positive lesions after 42 to 45 days
(IV) 137	(Control)				Negative; animals remained well
Normal rabbit	137				Positive lesions after 38 to 44 days

*In all of these protocols, the Roman numeral enclosed in brackets refers to the generation of the given strain of *Spirochaeta pallida* which was employed for experimental inoculation.

Experiment 8.—A series of rabbits was inoculated with Strain 117 which was isolated from the semen of a case of latent syphilis. The serums from a number of these animals were tested against a heterologous strain, No. 169. Protective substances were found in serums from six to fourteen months after infection, for homologous and heterologous *Spirochaeta pallida*.

TABLE 8.—RESULTS IN EXPERIMENT 8

Serum	Test Strain of <i>S. pallida</i>	Days Positive for <i>S. pallida</i>	Days Negative When Bled	Days Since Infection	Result
(II) 117	117	91	117	402	Protection; animals remained well
(III) 117	117	Spirochetes could not be found in dark-field examinations		270	Protection; animals remained well
(III) 117	117, 169	25	146	197	Protection; animals remained well
(III) 117	117	18	156	197	Protection; animals remained well
(IV) 117	117, 169	12	123	160	Protection; animals remained well
Normal rabbit	117				Positive lesions after 28 to 34 days

The next experiment shows in a more definite manner the difference between serums from animals in a state of infection approximating latency and those that have not yet reached that condition. There is, moreover, a distinct difference

seen in the outcome of the test when a heterologous strain of spirochetes is used, thus contrasting with the serums from rabbits which had been inoculated with latent strains.

TABLE 9.—RESULTS IN EXPERIMENT 9

Serum	Test Strain of <i>S. pallida</i>	Days Positive for <i>S. pallida</i>	Days Negative When Bled	Days Since Infection	Result
(I) 170	170	42	61	143	Positive lesions after 20 to 25 days
(I) 170	(Control)				Negative; animals remained well
(I) 170	170	42	138	220	Protection; animals remained well
(II) 170	170	7	36	77	Positive lesions after 34 days
(II) 170	(Control)				Negative; animals remained well
(III) 170	170	15	47	92	Positive lesions, 50 days
(III) 170	170	15	200	245	Protection; animals well
(III) 170	169	15	200	245	Positive lesions; 36 days
(IV) 170	170	13	0	33	Positive lesions after 27 days;
(IV) 170	(Control)				Negative; animals remained well
(IV) 170	170	13	166	199	Protection; animals remained well
(IV) 170	169	42	109	171	Positive lesions after 36 days
(VIII) 170	170	6	198	276	Protection; animals remained well
(X) 170	170	24	121	172	Protection; animals remained well
(VI) 169	169	24	152	199	Protection; animals remained well
Normal rabbit	169, 170				Positive lesions after 29 to 31 days

The conclusion which may be drawn from these results is that serums from rabbits experimentally infected with syphilis are uniformly negative for spirocheticidal properties except in those instances in which the infection has attained a relatively latent state which corresponds roughly to conditions in human syphilis.

DISCUSSION

The foregoing experiments have shown that latent syphilis in man is associated with a spirocheticidal property in the serum. This specificity is manifested at a time when the individual is outwardly free from the disease and appears to be well. When the infection is still active or is of recent origin, the protective element is not present in the serum. Substantially the same results are obtained with experimentally infected rabbits.

These observations would tend to confirm the belief that a true immunity does obtain at some time in the course of syphilitic infection. A state of latency would imply a balance that has been struck between the antibodies in an infected person and the invading spirochetes. The presence of *Spirochaeta pallida* in latent syphilitic persons⁹ is additional evidence in support of this idea. During that stage the spirochetes are innocuous for the host.

Immunity, in any sense, need not imply a condition which is incompatible with the life of a parasite. Resistance on the part of the host may be nicely balanced against that of the organism which continues to exist in certain surroundings without giving rise to manifestations characteristic of the disease. There are striking analogies in trypanosome infections, spirillary diseases and the carrier state in well-known diseases, such as typhoid and malaria.

The cyclic changes in syphilis are associated with reactions which point to a progressively increasing immunity on the part of the tissues. In the tertiary stage there is evidence of immunity in the paucity of *Spirochaeta pallida* in gummatous lesions and in the manifestations which conform to characteristic sensitization phenomena. A counterpart may be found also in tuberculosis and glanders. The mechanism by which immunity in syphilis develops would seem to be an elaboration of antibodies which is progressive and commences at the time when initial lesions are present. This begins as a local immunity reaction which extends from one group of tissues to another with a corresponding elaboration of specific substances into the blood. There is considerable evidence to support this view in some recent work¹¹ which has shown that a definite effect is exerted by one group of tissues on another in the production of clinical types of syphilis in the rabbit. The inhibitory effect of one local lesion on the development of lesions elsewhere has been mentioned by Nichols⁷ and more recently by Brown and Pearce.⁸

Failure to reinoculate with syphilis has been taken to mean existing disease rather than a state of immunity. This view, which has gained credence through Neisser and his school, can be interpreted from a different angle by supplementing the older facts with newer ones. The presence of *Spirochaetae pallidae* in organs and tissues of the body appears to be coexistent with immunity to reinfection in exactly the same sense as this occurs in piroplasmoses and trypanosome diseases. The immunity in these infections persists as long as the parasites are present, and the serum in some degree is known to have protective antibodies. In a similar manner, the presence in the human or animal body of *Spirochaetae pallidae* possessing full virulence when inoculated into new soil need not signify disease, but rather a latent stage in which the spirochetes are able to survive in the immunized body. The reaction which takes place is a reversible one, and it is likely that failure to reinfect with syphilis means simply the entry of spirochetes into surroundings which favor lodgment of organisms without the setting up of visible lesions or manifestations of a definite kind.

The old conception of immunity in syphilis was based on meager if not erroneous knowledge as to the mechanism of infection, the

dissemination of the spirochetes, and what was meant by generalization of the disease. More recent experimental study along these lines (Eberson,⁹ Brown and Pearce¹⁰) has given a different cast to immunity phenomena. Early dissemination of *Spirochaeta pallida* makes possible an early absorption of antibodies, until with the lapse of sufficient time, these accumulated products are discharged into the blood stream from different parts of the body where the spirochetes may have lodged. The blood immunity, which appears to prevail when syphilis is unequivocally latent, is a progressive development of an extensive tissue immunity which has been produced gradually in the infected person.

SUMMARY AND CONCLUSIONS

The blood serum from persons having latent syphilis was found to have spirocheticidal properties. Rabbits were protected uniformly against infection with virulent *Spirochaeta pallida* in combination with such serums.

Protective properties were found in the serums of asymptomatic persons with latent syphilis with the following histories:

Infection with syphilis dating back from three to twenty-five years.

Patients who had received treatment until the Wassermann reaction had become negative.

A number of patients who had no history of infection, who had taken no treatment, and who had a slightly positive Wassermann reaction usually in the cholesterin antigen.

A group of patients in whom the Wassermann reaction was slightly positive in the cholesterin and noncholesterin antigens, or strongly positive in either one, in inverse relationship.

An infant whose mother's serum was found to contain spirocheticidal properties.

Spirocheticidal activity of serums in latent syphilis is of such a character as to prevent the normal dissemination of *Spirochaeta pallida* from a primary focus. Failure to inoculate rabbits with mixtures of serums and spirochetes was correlated with negative inoculations with the blood from such animals.

In the experimental animal, spirochetolytic serum may be developed in the course of six months to one year after the infection. In the rabbit, as in man, protective substances are found at a time when the infection has attained a relatively latent state.

The presence of these substances in given serums apparently depends on the stage of infection. When definite latency has been established, the serum appears to protect against experimental inoculation, whereas the serum from cases of early syphilis or those in which true latency has not been attained is not spirocheticidal.

Spirocheticidal activity is essentially a function of time and depends on the degree to which the individual has elaborated and distributed the slowly accumulating antibodies.

Serums which were developed in rabbits by strains of *Spirochaeta pallida* from latent sources manifested a wider range of protective properties, as shown by the inhibitory effect on heterologous as well as homologous strains. Serums from latent cases behaved similarly. Chancre strains when used for experimental infection were not capable of developing spirocheticidal serums for heterologous organisms, in the few experiments which were attempted.

A negative Wassermann reaction following antisyphilitic treatment may or may not go hand in hand with spirocheticidal activity of serums. Continued treatment which renders a Wassermann reaction negative does not appear to nullify any existing protective property of the given serum.

By analogy with trypanosome and spirillary diseases and the carrier state of certain well-known infections, syphilis offers immunity phenomena which tend to explain latency on the basis of a blood immunity which is developed progressively from tissue immunity.

The mechanism by which immunity in syphilis develops would seem to be an elaboration of antibodies commencing at the time when initial lesions are present and continuing as a progressive extension of local immunity from one group of tissues to another until the immune substances are absorbed by the blood stream. Latent *Spirochaeta pallida* thus become innocuous for the host.

The presence of *Spirochaeta pallida* at certain times in the human or animal body need not imply disease but rather a latent stage in which the spirochetes are able to survive in the immunized body. Failure to reinfect with syphilis means, from this point of view, the entry of spirochetes into surroundings which favor lodgment without setting up of visible lesions or manifestations. Immunity need not imply a condition which is incompatible with the life of a parasite. Latency, then, connotes a balance that has been struck in the individual between the antibodies and the invading parasites.

The results of the experiments reported in this paper suggest that the serum from definitely established latent cases of syphilis may prove of therapeutic value.³¹

31. In addition to the references given, the following may be of interest:

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Brown, W. H., and Pearce, L.: J. Exper. M. **31**:729, 1920; **32**:473, 1920.

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- Landsteiner: *Centralbl. f. Bakteriol., Ref. Abt. 1* **41**:785, 1908.
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Uhlenhuth and Mulzer: *Arb. d. k. Gsndhtsamte* **44**:307, 1913.
Zinsser, Hans, and Hopkins, J. Gardner: The Viability of the *Spirochaeta Pallida* in Diffuse Light at Room Temperature, *J. A. M. A.* **62**:1802 (June 6) 1914; *J. Exper. M.* **21**:576, 1915.

REFRACTOMETRIC STUDIES IN HUMAN SYPHILIS WITH SPECIAL REFERENCE TO CHANGES DURING TREATMENT WITH ARSPHENAMIN AND NEO-ARSPHENAMIN*

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INTRODUCTION

The refractometric studies with the proteins of the serum in syphilis reported in this article were undertaken at the suggestion of Prof. John A. Kolmer as primarily bearing on the nature of the serum changes in this disease in relation to immunologic phenomena and as possibly yielding additional information as to the mechanism of the "reactions" sometimes developing after the intravenous injection of solutions of arsphenamin and neo-arsphenamin.¹ Various hypotheses have been advanced in explanation of these "reactions," among which those based on the formation of precipitates in vivo have attracted considerable attention. Berman² believes that precipitates may be produced because of the presence of an excess of serum globulins in the plasma, and advocates a simple test for determining whether or not the serum of a patient produces precipitates with alkalinized solutions of arsphenamin in vitro.

Schamberg, Tokuda and Kolmer,³ however, found that the test is without practical value and that the production of precipitates in vitro in this test is directly influenced by the amount of alkali present in the solutions of arsphenamin and neo-arsphenamin.

REVIEW OF LITERATURE

A number of investigators have found that when animals are immunized with bacteria, toxins and proteins, an increase in the serum globulins takes place.

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*Investigation aided by funds accruing from the preparation of arsphenamin.

1. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Weiss, C.: Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin, *Arch. Dermat. & Syph.* **1**:235-255 (March) 1920.

2. Berman.: The Nitrotoid Crisis After Arsphenamin Injections, *Arch. Int. Med.*, 1918. **22**:217-224, (Aug.) 1918.

3. Schamberg, J. F.; Tokuda, K., and Kolmer, J. A.: A Study of Arsphenamin Serum Precipitates and Their Relation to Clinical Reactions, *Arch. Dermat. & Syph.* **3**:263 (March) 1921.

Rowe ⁴ found that in all infections, except acute tonsillitis, typhoid fever and certain mild infections, the globulins were definitely increased. The globulins are also increased in syphilis. There is, however, no direct relation between the substance ("reagins" of "antibodies") which give rise to the Wassermann reaction and the increase of the globulins. Rowe reports that in syphilis the average value of globulins is definitely *increased* over the normal value, while that for nonprotein constituents is only very slightly increased. In a case in which the clinical diagnosis of the early lesion was chancre, the percentage of globulin was found to be normal, but in particularly severe cases of syphilis, the percentage of globulin was found to be the highest.

Winternitz ⁵ found that serum globulins were moderately increased in syphilis.

Elias, Neubauer, Porges and Salomon ⁶ thought the active substance causing the Wassermann reaction belonged to the globulins, and that they were present in greater amount in syphilis than in normal serum.

Noguchi ⁷ and other investigators also found that the globulins are increased in syphilis.

Hurwitz and Meyer ⁸ found that the progress of bacterial infections in experimental rabbits is usually associated with an *increase* of the globulin, provided the infection is severe; a mild chronic infection may continue for a long time without causing a marked change in the relation of the serum protein. Immunization with carefully controlled doses could be attained without a decided increase of globulins. Ordinarily when an animal reacts severely, the globulin is increased.

E. S. Schmidt and C. L. A. Schmidt ⁹ report that a decrease of serum proteins followed the injection of benzene (benzol), though no change occurred in the protein quotient.

Cervello ¹⁰ reports that after administering antipyriu to dogs, he finds an increase of both globulins and of total proteins.

4. Rowe, A. H.: Refractometric Studies of Serum Proteins in Nephritis, Cardiac Decompensation, Diabetes, Anemia, and Other Chronic Diseases, Arch. Int. Med., **19**:354-366, (March) 1917.

5. Winternitz, R.: Ein Beitrag zur chemischen Untersuchung des Blutes rezent leutischer Menschen, Arch. f. Dermat. u. Syph. **93**:65-72, 1908.

6. Elias, H.; Neubauer, E.; Porges, O., and Salomon, H.: Theoretisches über die Serumreaktion auf Syphilis, Wien. klin. Wchnschr. **21**:748-752, 1908.

7. Noguchi, H.: The Relation of Protein, Lipoid and Salts to the Wassermann Reaction, J. Exper. Med., **11**:84-99, 1909.

8. Hurwitz, S. H., and Meyer, K. F.: I. The Serum Globulin in Bacterial Infection and Immunity, J. Exper. Med. **24**:515-546 (Nov.) 1916.

9. Schmidt, E. S., and Schmidt, C. L. A.: On the Noninfluence of Injections Upon the Proteins of Globulin and Albumin in Blood Serum, J. Immunology, **2**:343 (June) 1917.

10. Cervello, C.: Einfluss der antipyretica auf die Albuminoide des Blutserums, Arch. f. exper. Path. u. Pharmakol. **10**, **62**:357-364, 1909.

Hurwitz and Whipple¹¹ found that the intoxication which develops after an acute or chronic obstruction of the intestine is in most instances associated with definite change in the blood proteins. In a simple obstruction with toxic death, the globulins may rise to double their initial value within forty-eight hours after the production of the obstruction. In the majority of such instances, the globulins continue high until death occurs. Similarly, animals with a chronic obstruction show a rise in the serum globulins. In these animals, the globulin increase takes place more slowly, but it may be of great magnitude and may show a tendency to return to its initial value.

Meyer, Hurwitz and Taussig¹² report that the percentage of serum globulins increases markedly during the course of immunization with diphtheria, tetanus, and botulinus toxin. In the case of botulinus toxin, however, there is first an initial rise in the albumin fraction.

These investigators found no constant relationship between the percentage increase in the serum globulin and the antitoxic potency of the serum. They conclude that the rise in globulins may be a manifestation of an upset in the delicate protein balance of the blood, resulting from the disturbed metabolism following the toxin inoculation.

Hurwitz and Meyer¹³ report that the progress of an infection is usually associated with marked changes in the serum proteins. There may be an increase in the percentage of the total proteins during some stage of the infection; there is usually a change in the albumin-globulin ratio with an increase in the total globulins. The nonprotein constituents of the blood show fluctuations with a tendency to rise as the infection progresses. Seng¹⁴ found increased globulin in serum from animals immune to diphtheria. Jakoby¹⁵ found the euglobulins increased in animals immunized to castor oil. Moll¹⁶ reports that in

11. Hurwitz, S. H., and Whipple, G. H.: Studies on the Blood Proteins. II. The Albumin-Globulin Ratio in Experimental Intoxication and Infections, *J. Exper. Med.*, **25**:231-253 (Feb.) 1917.

12. Meyer, K. F.; Hurwitz, S. H., and Taussig, L.: Studies on the Blood Proteins. III. Albumin-Globulin Ratio in Antitoxic Immunity, *J. Infect. Dis.*, **22**:1-27 (Jan.) 1918.

13. Hurwitz, S. H., and Meyer, K. F.: Studies on the Blood Proteins I. The Serum Globulins in Bacterial Infection and Immunity, *J. Exper. Med.*, **24**: 515-545 (Nov.) 1916.

14. Seng, W.: Über die qualitativen und quantitativen Verhältnisse der Eiweisskörper im Diphtherieheilserum, *Ztschr f Hyg. u. Infektionskrankh*, **31**: 513-532, 1899.

15. Jakoby, M.: Über Ricin-Immunität, *Beitr. z. chem. Phys. u. Path.*, **1**:51-77, 1901-1902.

16. Moll, L.: Über künstliche Umwandlung von Albumin in Globulin, *Beitr. z. chem. Phys. u. Path.* **4**:563-577, 1903; Über Blutveränderungen nach Eiweissinjektionen, *ibid.* **4**:578-589, 1903.

animals injected with various proteins, including gelatin and killed bacteria, a marked increase in the globulin content occurs, and he concludes that an increase in immune bodies is associated with an increase in the globulins. Langstein and Mayer¹⁷ report that the serum proteins are increased in immunized and infected rabbits, the increase being largely in the globulin fraction.

SCOPE OF THIS INVESTIGATION

The subjects studied in this part of our investigation were:

1. A comparison of the values of the refractometric index of the serum and of the percentage of serum albumin and serum globulin in normal human serums (collected from the literature) with the values found in *untreated* human syphilis (author's observations) during the various stages of the disease.
2. A comparison of the changes in the blood serum of patients with syphilis in relation to the Wassermann reaction before treatment.
3. The changes in the refractometric index and in the percentage of serum proteins during the course of treatment with arsphenamin; patients classified according to their degree of resistance to antisypilitic treatment.
4. The changes during treatment with neo-arsphenamin.

MATERIALS AND METHODS OF INVESTIGATION

All the determinations of the albumin, globulins and nonprotein constituents of the blood of syphilitic patients were made by the microrefractometric method of Robertson.¹⁸ The Pulfrich refractometer was used and the percentages of the various constituents were calculated in all cases in the manner presented in detail by Robertson. The tests were made with sodium light.

All the arsphenamin and neo-arsphenamin used in these experiments was produced at the Dermatological Research Institute, Philadelphia. These drugs were injected intravenously in the treatment of syphilitic patients at intervals of from three to four or seven days by the following method:

Arsphenamin (dose from 0.4 to 0.6 gm.) was dissolved in distilled water (from 80 to 120 c.c.) and neutralized with a sufficient amount of sodium hydroxid to produce the disodium salt, as described by Schamberg, Kolmer, Raiziss and Weiss.¹ The injections were made

17. Langstein, L., and Mayer, M.: *Über das Verhalten der Eiweisskörper des Blutplasmas bei experimentellen Infektionen*, Beitr. z. chem. Phys. u. Path. **5**:69-82, 1904.

18. Robertson, T. B.: *A Microrefractometric Method of Determining the Percentages of Globulin and Albumin in Very Small Quantities of Blood Serum*, J. Biol. Chem. **22**:233-239, 1916.

by means of a gravity apparatus. Neo-arsphenamin (dose 0.9 gm.) was injected in a volume of 10 c.c. of distilled water with the use of a Luer syringe. No extra alkali was added.

Blood was obtained from the median basilic vein in every case just before an injection. Two sterile test tubes were used for collecting the blood, the first, for the Wassermann reaction, and the second

TABLE 1.—REFRACTOMETRIC DETERMINATIONS ON HUMAN SERUMS IN VARIOUS STAGES OF UNTREATED SYPHILIS

Case	Sex*	Age	Clinical Diagnosis	Wassermann Reaction	Refractometric Index	Percentage of			Relative Amounts of	
						Total Proteins	Albumin	Globulin	Albumin	Globulin
15	♂	11	Congenital.....	++++	1.34924	5.71	5.38	0.33	94	6
14	♂	14	Congenital.....	++++	1.35036	6.64	5.83	0.81	88	12
16	♂	17	Congenital.....	++++	1.35010	6.66	4.54	1.52	74	26
R 1†	♂	19	Primary.....	7.60	6.40	1.20	84	16
4	♂	19	Secondary.....	++++	1.35036
13	♂	20	Secondary.....	++++	1.35197	7.11	6.14	0.97	86	14
22	♂	21	Secondary.....	++++	1.35106	7.19	5.69	1.50	79	21
24	♂	21	Secondary.....	++++	1.35045	6.96	5.38	1.58	77	23
5	♂	24	Secondary.....	++++	1.35509
11	♂	26	Secondary.....	++++	1.35236	7.51	5.19	2.32	69	31
8	♂	28	Secondary.....	++++	1.35132	7.28	5.66	1.62	78	22
2	♂	28	Secondary.....	++++	1.35045	7.28	5.90	1.38	81	19
27	♂	30	Secondary.....	++	1.35113
12	♂	31	Secondary.....	++++	1.35097	6.97	5.49	1.48	79	21
10	♂	32	Secondary.....	++++	1.35053	6.66	5.53	1.13	83	17
31	♂	37	Secondary.....	++	1.35002	6.02	4.36	1.66	72	28
28	♂	38	Secondary.....	++	1.35088	7.01	5.62	1.39	80	20
9	♂	45	Secondary.....	++++	1.35071	6.34	4.46	1.88	70	30
3	♂	50	Secondary.....	++++	1.35036	6.70	4.85	1.85	72	28
25	♂	19	Secondary.....	++++	1.35810	10.12	5.61	4.51	55	45
32	♂	23	Secondary.....	++	1.35245
30	♂	23	Secondary.....	++	1.35149
18	♂	25	Secondary.....	++++	1.35123	6.96	5.62	1.32	81	19
19	♂	25	Secondary.....	++++	1.35026	6.70	5.62	1.08	84	16
23	♂	26	Secondary.....	++++	1.35342	7.97	6.26	1.71	78	22
21	♂	29	Secondary.....	++++	1.35002	6.53	5.39	1.14	82	18
33	♂	38	Secondary.....	++	1.35026	6.03	5.24	0.79	87	13
20	♂	40	Secondary.....	++++	1.35079	7.07	5.81	1.26	82	18
1	♂	41	Secondary.....	++++	1.35210	7.53	6.47	1.06	86	14
R 2	♂	..	Early secondary	—	7.60	5.30	2.30	70	30
R 3	♂	..	Early secondary	+++	7.90	4.60	3.30	58	42
R 4	♂	..	Early secondary	+++	7.40	5.40	2.00	73	27
R 5	♂	..	Early secondary	+++	8.30	6.10	2.20	73	27
R 8	♂	..	Early secondary	+++	7.30	3.70	3.60	51	49
R14	♂	..	Secondary.....	+++	8.10	5.20	2.90	64	36
R18	♂	..	Late secondary..	+++	7.30	5.40	1.90	74	26
R13	♂	..	Tertiary.....	+++	7.10	4.60	2.50	65	35
R15	♂	..	Tertiary.....	+	7.40	4.50	2.90	61	39
29	♂	50	Tertiary.....	++	1.34829	5.78	5.08	0.70	88	12
17	♂	70	Tertiary.....	++++	1.35045	6.77	5.66	1.71	75	25
7	♂	42	Tabes.....	++++	1.35105	7.20	5.79	1.41	80	20
6	♂	54	Tabes.....	++++	1.35184	7.58	5.91	1.67	78	22
G—	♂	20	+	1.35000
G—	♂	26	+	1.35140

* In this column and in the following tables, ♂ represents male, and ♀ female.

† R indicates cases taken from the paper of Rowe; G indicates cases taken from the paper of Gettler and Baker; all other cases are the author's.

for the refractometric investigations. We thus prevented traces of water or alcohol which might have remained in the needle from getting into the blood and vitiating the refractometric determinations. The specimens, in stoppered test tubes, were kept in the refrigerator over night, and were centrifugalized the next morning to obtain clear serum, which was studied.

The cases were patients with untreated syphilis from the clinic of Dr. Jay F. Schamberg, Polyclinic Hospital, Graduate School of Medicine, University of Pennsylvania, Philadelphia. The urine of each patient was regularly examined and injections were made only when no albumin was demonstrable.

THE REFRACTIVE INDEX AND PERCENTAGE OF SERUM PROTEINS
IN SYPHILITIC BLOOD SERUM COMPARED WITH NORMAL SERUM

In order to aid in the interpretation of our results, we have collected from the literature all the available data on refractometric studies on human blood under normal conditions as well as in syphilis, and have compared these figures with our own observations on *untreated* syphilitic cases. A summary of these data is presented in Tables 1 and 2.

From the work of Rowe¹⁹ we have the following data as to the range of the serum proteins in a series of twenty-two normal human cases: Albumin varies between 4.5 and 6.7 per cent., with an average value of 5.6 per cent.; globulin varies between 1.2 and 2.3 per cent., with an average value of 1.9 per cent.; total proteins between 6.5 and 8.2 per cent., average value 7.5 per cent.; relative amount of globulin 16 to 32 per cent., average value 25.5 per cent.

Gettler and Baker²⁰ in their refractometric studies on a series of twenty-eight *normal* cases give the limits of variation of the refractive index (ND) from 1.34900 to 1.35210, with an average value of 1.35045. (These figures have been obtained by converting their figures to the Robertson system by the addition of 1.33320—the refractive index of water. Any changes arising from this correction should be slight and should not affect the conclusions drawn from them.)

With these normal figures as a basis of comparison, we may now turn to the subject of syphilis. Our own values based on a series of thirty-two untreated cases may be summarized as follows: The refractometric index varies between 1.34829 and 1.35810, the average value being 1.35123. The percentage of total proteins varies between 5.78 and 10.12 per cent., the average being 6.95 per cent. Percentage of albumin ranges from 4.36 to 6.47 per cent., average 5.48 per cent.; globulin from 0.33 to 4.51 per cent., average 1.47 per cent.; relative amount of albumin from 55 to 94 per cent. of the total proteins, average value 79 per cent.; relative amount of globulin varies from 6 to 45 per cent. of the total proteins, the average being 21 per cent.

19. Rowe, A. H.: The Albumin and Globulin Content of Human Blood Serum, *Arch. Int. Med.*, **18**:455-473 (Oct.) 1916.

20. Gettler, A. O., and Baker, W.: Chemical and Physical Analysis of Blood in Thirty Normal Cases, *J. Biol. Chem.* **25**:211-222 (June) 1916.

Rowe's results in syphilis (based upon ten untreated cases) are as follows: The total proteins varied between 7.1 and 8.3 per cent., the average being 7.6 per cent.; albumin varied between 3.7 and 6.4 per cent., average 5.12 per cent.; globulins between 1.2 and 3.6 per cent., average, 2.48 per cent.; relative amount of globulin varied between 16 and 49 per cent. of the total proteins, averaging 37.3 per cent.

Gettler and Baker in two cases with positive Wassermann reactions give the value for refractive index as 1.35090 and 1.35140.

It is evident, if we compare figures, that there is a marked increase in the refractometric index of the serum in syphilis, *especially in active*

TABLE 2.—SUMMARY OF REFRACTOMETRIC DETERMINATIONS IN UNTREATED HUMAN SYPHILIS: AVERAGE VALUES OF AUTHOR'S SERIES (THIRTY-TWO CASES)

	Refractometric Index	Percentage of			Relative Amounts of	
		Total Proteins	Albumin	Globulin	Albumin	Globulin
Average values of entire series.....	1.35123	6.95	5.48	1.47	79	21
Limits of variation from.....	1.34829	5.78	4.36	0.33	55	6
to.....	1.35810	10.12	6.47	4.51	94	45
Average of three congenital cases.....	1.34990	6.13	5.24	0.89	86	14
Average of twenty-five secondary cases.....	1.35152	7.44	5.87	1.57	79	21
Average of four tertiary cases.....	1.35041	6.83	5.46	1.37	80	20
Average and range of values of refractive index and serum proteins classified according to the Wassermann reactions of the serums						
Wassermann reaction ++++ (25 cases)	1.35126	7.00	5.55	1.45	79	21
Limits of variation from.....	1.34924	6.02	4.36	0.33	55	6
to.....	1.35810	10.12	6.47	4.51	94	45
Wassermann reaction ++ (7 cases).....	1.35065	6.35	5.07	1.28	80	20
Limits of variation from.....	1.34829	5.78	4.36	0.70	72	12
to.....	1.35245	7.01	5.62	1.66	88	28
Average of values of Rowe's series (10 cases)						
Average.....	7.60	5.12	2.48	68	32
Limits of variation from.....	7.10	3.70	1.20	51	16
to.....	8.30	6.40	3.60	84	49

secondary cases. The total proteins show a similar change, the increase being in globulins.

When we compare our values with those of Rowe for syphilis, we observe that the number of cases in our series being much greater, our range of total proteins is much wider, giving us a somewhat lower average. Our albumin average is somewhat higher. The variation in the globulins is much greater in our series and our average is much lower; the range of the relative amounts of globulin obtained by us is also much greater but our average is much lower.

If we classify our results according to the stages of syphilis, we see that the refractive index of the serum is highest in secondary cases, lowest in the congenital cases and is intermediate between these two in the tertiary cases. The figures for total proteins, albumins, globulins

and the relative amount of globulins are somewhat higher in secondary than in tertiary syphilis, the figures for congenital syphilis being somewhat lower than those of the latter.

If we compare these classified results with those of Rowe, we observe that our values of total proteins, albumin, globulin, and the relative amount of globulin in *tertiary syphilis* are lower. In secondary syphilis our values of total proteins, globulin, and the relative amount of globulin are lower.

Considering now the Wassermann reaction of the serum, we note that in the *strongly positive* cases, the values of total proteins, albumin,

TABLE 3.—AVERAGES OF THE CHANGES IN THE ALBUMIN, GLOBULIN, AND TOTAL PROTEIN CONTENT OF THE BLOOD SERUM OF SYPHILITICS

	Refractometric Index	Percentage of			Relative Amounts of	
		Total Proteins	Albumin	Globulin	Albumin	Globulin
Series A. Cases yielding strongly positive Wassermann reactions						
Before injection.....	1.35126	7.00	5.55	1.45	79.3	20.7
After 1st injection.....	1.35096	6.97	5.54	1.43	79.5	20.5
After 2d injection.....	1.35059	6.70	5.40	1.30	80.6	19.4
After 3d injection.....	1.35065	6.69	5.43	1.26	81.2	18.8
After 4th injection.....	1.35073	6.97	5.60	1.37	80.3	19.7
After 5th injection.....	1.35078	6.93	5.59	1.34	80.7	19.3
After 6th injection.....	1.35061	6.83	5.53	1.30	81.0	19.0
After 7th injection.....	1.35053	6.83	5.54	1.29	81.1	18.9
After 8th injection.....	1.35049	6.86	5.50	1.36	80.2	19.8
Series B. Cases yielding weakly positive Wassermann reactions						
Before injection.....	1.35065	6.35	5.07	1.28	79.8	20.2
After 1st injection.....	1.35025	6.39	4.98	1.41	77.9	22.1
After 2d injection.....	1.34926	5.98	4.72	1.26	78.9	21.1
After 3d injection.....	1.35054	6.67	5.33	1.34	79.9	20.1
After 4th injection.....	1.35047	6.42	5.04	1.38	78.5	21.5
After 5th injection.....	1.34973	6.56	5.32	1.24	81.1	18.9
After 6th injection.....	1.34985	6.34	5.14	1.20	81.1	18.9
After 7th injection.....	1.35028	6.74	5.49	1.25	81.5	18.5
After 8th injection.....	1.35045	7.02	5.69	1.33	81.1	18.9

globulin, and the relative amount of globulin are higher than those in the *weakly positive* cases.

The weakly as well as the strongly positive cases in our series show values for total proteins, globulin, and the relative amounts of globulin lower than those of Rowe, the values for the albumin of the strongly positive series being somewhat higher. In the weakly positive cases, our values of albumin are lower.

THE CHANGES OCCURRING IN SYPHILIS DURING TREATMENT WITH ARSPHENAMIN AND NEO-ARSPHENAMIN

1. *A Comparison of the Changes in Refractive Index and Serum Proteins During Arsenical Treatment; Patients Classified According to the Wassermann Reaction of the Serums Before Treatment.*—As will be seen from Table 3, the curve of the refractive indexes of the

strongly positive serums shows a fairly progressive downward course throughout the period of treatment. The weakly positive serums, on the other hand, show very irregular fluctuations throughout treatment.

The percentage of total proteins shows little or no change during the course of treatment in the strongly positive cases and tends to increase somewhat irregularly in the weakly positive cases.

TABLE 4.—AVERAGES OF REFRACTOMETRIC CHANGES DURING ARSENICAL TREATMENT CLASSIFIED ACCORDING TO INTERVAL OF INJECTIONS

	Refractometric Index	Percentage of			Relative Amounts of	
		Total Proteins	Albumin	Globulin	Albumin	Globulin
1. Arsphenamin, 7 day intervals						
Before injection.....	1.35081	6.82	5.19	1.63	76	24
After 1st injection.....	1.35007	6.70	5.02	1.68	75	25
After 2d injection.....	1.35006	6.35	4.87	1.48	76	24
After 3d injection.....	1.35055	6.54	5.11	1.43	78	22
After 4th injection.....	1.35018	6.69	5.25	1.44	78	22
After 5th injection.....	1.35045	6.86	5.43	1.43	79	21
After 6th injection.....	1.35041	6.87	5.51	1.36	80	20
After 7th injection.....	1.35011	6.54	5.38	1.16	82	18
After 8th injection.....	1.35011	6.62	5.26	1.36	80	20
2. Arsphenamin, 3 or 4 day intervals						
Before injection.....	1.35135	7.13	5.40	1.73	76	24
After 1st injection.....	1.35177	7.28	5.61	1.67	77	23
After 2d injection.....	1.35004	6.76	5.31	1.45	78	22
After 3d injection.....	1.35051	6.53	5.20	1.33	79	21
After 4th injection.....	1.35011	6.97	5.45	1.52	78	22
After 5th injection.....	1.35210	7.43	5.71	1.71	77	23
After 6th injection.....	1.35101	6.92	5.34	1.58	77	23
After 7th injection.....	1.35023	6.91	5.34	1.57	77	23
After 8th injection.....	1.35173	7.42	5.76	1.66	78	22
3. Neo-arsphenamin, 7 day intervals						
Before injection.....	1.35121	6.87	5.70	1.17	83	17
After 1st injection.....	1.35007	6.89	5.72	1.17	84	16
After 2d injection.....	1.35050	6.72	5.54	1.18	82	18
After 3d injection.....	1.35071	6.78	5.64	1.14	83	17
After 4th injection.....	1.35104	7.00	5.74	1.26	82	18
After 5th injection.....	1.35039	6.05	4.92	1.13	83	17
After 6th injection.....	1.35041	6.66	5.55	1.11	83	17
After 7th injection.....	1.35071	6.90	5.79	1.11	84	16
After 8th injection.....	1.35039	6.91	5.76	1.15	83	17
4. Neo-arsphenamin, 3 or 4 day intervals						
Before injection.....	1.35106	6.86	5.35	1.51	78	22
After 1st injection.....	1.35038	6.49	5.08	1.41	78	22
After 2d injection.....	1.34996	6.65	5.41	1.24	81	19
After 3d injection.....	1.35057	6.90	5.60	1.29	81	19
After 4th injection.....	1.35042	6.88	5.50	1.38	80	20
After 5th injection.....	1.35033	6.65	5.12	1.53	80	20
After 6th injection.....	1.35068	6.80	5.42	1.38	80	20
After 7th injection.....	1.35077	6.86	5.48	1.48	79	21
After 8th injection.....	1.34999	6.64	5.33	1.31	80	20

The percentage of albumins shows an initial tendency to decrease in the strongly positive cases and gradually increase in the weakly positive. The globulins in the weakly positive series show an increase with the first injection and then fluctuate. In the strongly positive series, the globulins continue to decline very slowly but rather irregularly.

The relative amounts of the globulins show only a slight tendency to decline in the strongly positive; in the weakly positive series there is practically no change until after the fourth injection; then follows

a fairly progressive decline. The relative amounts of albumin tend to increase more uniformly in the strongly positive than in the weakly positive series.

2. *The Changes in the Refractive Indexes and Serum Proteins of Syphilis Serums of Patients Treated With Arsphenamin and Neo-Arsphenamin, Classified According to the Interval of Injections.*—(A) Weekly Intervals: The refractive index of the serum, when treatment with arsphenamin was given at seven day intervals, showed a marked drop after the first two injections then a rise and finally a gradual decline (Table 4.)

The refractive index when neo-arsphenamin was used shows a somewhat similar curve.

TABLE 5.—AVERAGE RESULTS OF TYPE I SERUMS *

	Refractometric Index	Percentage of			Relative Amounts of	
		Total Proteins	Albumin	Globulin	Albumin	Globulin
Type I serums						
Before injection.....	1.35089	6.97	5.41	1.57	77.6	22.4
After 1st injection.....	1.35144	7.12	5.51	1.61	77.4	22.6
After 2d injection.....	1.35048	6.72	5.32	1.40	79.2	20.8
After 3d injection.....	1.35067	6.63	5.25	1.38	79.2	20.8
After 4th injection.....	1.35064	6.96	5.45	1.50	78.3	21.7
After 5th injection.....	1.35076	6.90	5.48	1.41	79.4	20.6
After 6th injection.....	1.35082	6.85	5.43	1.43	79.3	20.7
After 7th injection.....	1.35063	6.88	5.41	1.49	78.6	21.4
After 8th injection.....	1.35088	6.99	5.52	1.52	79.0	21.0
Type II serums						
Before injection.....	1.35074	6.64	5.19	1.45	76.7	23.3
After 1st injection.....	1.35040	6.48	5.02	1.47	77.5	22.5
After 2d injection.....	1.35016	6.41	5.00	1.41	78.0	22.0
After 3d injection.....	1.35067	6.76	5.40	1.38	79.9	20.1
After 4th injection.....	1.35080	6.50	5.41	1.37	83.2	16.8
After 5th injection.....	1.35096	6.95	5.48	1.45	78.8	21.2
After 6th injection.....	1.35070	6.85	5.43	1.43	79.3	20.7
After 7th injection.....	1.35060	6.76	5.49	1.27	81.2	18.8
After 8th injection.....	1.35051	6.88	5.45	1.44	79.2	20.8

* Type I Serums: Cases strongly resisting antisyphilitic treatment. Type II Serums: Cases yielding readily to antisyphilitic treatment.

The percentages of total proteins and albumins under either arsphenamin or neo-arsphenamin treatment show curves which have something in common. There is a general tendency for the curves to fall after the first two injections; this is followed by a gradual rise above normal level about the fifth week, and after this rise the curves fluctuate.

The relative amounts of globulin show more rapid decline during weekly arsphenamin than neo-arsphenamin injections.

(b) Semiweekly Intervals: The series which was treated with arsphenamin at three or four day intervals shows curves somewhat different from the foregoing. The refractive index of the serum increases

slightly after the first injection, decreases rapidly after the second injection, and then the curve rises and falls irregularly.

In the cases which were treated with neo-arsphenamin, the refractive index drops fairly continuously after the first and second injection, rises slightly at the third injection and then remains practically unchanged.

The percentage of total proteins and albumins fluctuated after injection of either arsphenamin or neo-arsphenamin.

The relative amounts of globulin show about the same tendency to decline under neo-arsphenamin as under arsenamin treatment.

3. *A Comparison of the Refractometric Changes in Syphilitic Serums During Arsenical Therapy; Cases Classified According to Their Degree of Resistance to Antisyphilitic Treatment.*—The syphilitic cases are classified in this discussion into two types according to the degree of resistance during the course of treatment. To the first type belong the cases which resisted the treatment strongly; that is,

TABLE 6.—SUMMARY OF DATA OF THE AUTHOR'S ENTIRE SERIES OF THIRTY-TWO CASES, SHOWING THE AVERAGES OF THE CHANGES OF THE REFRACTIVE INDEX AND PROTEINS OF THE SERUM DURING THE COURSE OF ARSENICAL TREATMENT

	Refractometric Index	Percentage of			Relative Amounts of	
		Total Proteins	Albumin	Globulin	Albumin	Globulin
Before injection.....	1.35123	6.95	5.48	1.47	79	21
After 1st injection.....	1.35081	6.83	5.44	1.44	79	21
After 2d injection.....	1.35027	6.57	5.28	1.29	80	20
After 3d injection.....	1.35063	6.78	5.41	1.27	80	20
After 4th injection.....	1.35008	6.88	5.51	1.37	80	20
After 5th injection.....	1.35006	6.90	5.57	1.33	81	19
After 6th injection.....	1.35054	6.78	5.49	1.29	81	19
After 7th injection.....	1.35050	6.81	5.53	1.28	81	19
After 8th injection.....	1.35049	6.81	5.53	1.28	81	19

the Wassermann reaction was persistently positive; and to the second type belong the cases in which the Wassermann reaction became negative very readily.

(a) *Refractive Index of Serum.*—In the first type the refractive index of the serum shows little or no tendency to drop below its original value. On the contrary, we note an increased value with the first injection.

In the third type, there is a decided fall after the first two injections, followed by high levels up to the sixth week and ending in a decline of the curve.

(b) *Total Proteins:* The changes in the percentage of total proteins are almost parallel to those of the refractive index in each of the two types.

(c) *Relative Amounts of Globulins.*—The relative amounts of globulin in the first type show only a very slight tendency to decrease during the course of treatment.

In the second type there is more tendency for the curve to fall during the course of treatment.

4. *General Survey of the Average Refractometric Changes in Syphilis During Arsenical Treatment.*—If we consider the averages of the refractometric changes during arsenical treatment of our entire series of thirty-two syphilitic cases, without special classification, we note the following (Table 6):

(a) The refractive index and percentage of total proteins of the serum show a tendency to decrease more or less regularly during a course of injections of arsphenamin or of neo-arsphenamin.

(b) The albumin content of the serum shows irregular fluctuations.

(c) The relative amounts of globulins diminish fairly progressively.

COMMENT

It is generally conceded that the disturbances in metabolism incident to infection by various micro-organisms, including *Spirochaeta pallida*, are manifested in part by an increase in the viscosity of the blood and therefore of the refractive index, the percentage and relative amounts of the various serum proteins. In syphilis, and perhaps also in other infections, it may be assumed that these increases are really due in part or entirely to an augmentation in the lipins (cholesterol, lecithin, etc.) which are bound in a strong chemical union with the serum proteins. This phenomenon is no doubt a manifestation of the response of the body to invasion and injury, in other words, it is a phase of the inflammatory process.

As for the possibility suggested by Berman² that an increase in the serum proteins bring about their precipitation by arsphenamin in vivo, we have not found any correlation in our studies between clinical reactions and refractometric changes. The severe reactions after arsphenamin injections are in our opinion due either to technical errors in administration or to the presence of certain unavoidable and unrecognizable impurities in the drugs. This has been fully discussed by Schamberg, Kolmer, Raiziss and Weiss.³

The serum proteins, functioning as they do primarily in controlling the viscosity of the blood and to only a minor degree in controlling its hydrogen-ion concentration, probably only serve an insignificant rôle in the syndrome known as the "nitrodoid reaction." We shall have to search for more injurious disturbances, such as the action of

arsphenamin on the suprarenals or those due to general tissue destruction or kidney injury, to explain the mechanism of the severe reactions often observed after intravenous injections of arsphenamin and neo-arsphenamin.

SUMMARY

The general conclusion drawn from a review of the recent literature on refractometric studies in syphilis and other infectious diseases seems to be that increases in the globulins of the serum accompany severe infections or acute intoxications.

Refractometric studies were made upon thirty-two cases of untreated syphilis and the following observations were made:

1. There is a marked increase in the refractive index of the serum and also in the globulins in syphilis, especially in active secondary cases. This confirms the findings of Rowe.

2. The refractive index of the serum is highest in secondary cases, lowest in the congenital and is intermediate between these two in the tertiary cases. The figures for total proteins, albumins, globulins and the relative amount of globulin are somewhat higher in secondary than in tertiary syphilis, the figures for congenital syphilis being somewhat lower than those of the latter.

3. Considered in relation to the Wassermann reaction of the serums, before treatment, the strongly positive cases show values of total proteins, albumins, globulins and relative amount of globulins higher than the weakly positive cases.

4. During a course of eight intravenous injections of arsphenamin (0.4 to 0.6 gm.) and neo-arsphenamin (0.9 gm.), each drug being given at weekly and semiweekly intervals, the refractometric studies (made before each injection) show these results:

5. Classified according to the Wassermann reaction of the serums before treatment, there are no sufficiently constant or striking differences to warrant differentiating between the strongly and weakly positive series.

6. Considered according to the intervals of injection, the relative amounts of globulins show more *rapid* decline during weekly arsphenamin than neo-arsphenamin injections.

During semiweekly periods of administration the changes are about the same.

7. Classified according to the degree of resistance of the patients to antisypilitic treatment (as indicated by repeated Wassermann tests) it was observed that: When the Wassermann reaction remained per-

sistently positive, the refractive index, the percentage of total proteins and the relative amount of globulins of the serum showed little or no tendency to drop below their original values. When the Wassermann reaction, on the other hand, became very readily negative, the curves fell, with more or less regularity during the course of injections.

STREPTOCOCCIC DERMATOSES *

ERNEST DWIGHT CHIPMAN, M.D.

SAN FRANCISCO

In the production of numerous dermatoses the streptococcus plays either a preponderant or an accessory rôle. In the one case, lesions result from the direct inoculation of the sound skin, giving rise to what may be considered a pure streptococcic dermatosis. In the other case, various complexes follow the inoculation of an antecedent affection, with the streptococcus either alone or in association with another organism.

As to what reactions may be properly classified as streptococcic in the strict sense, there is probably some divergence of opinion. Of course the simple occurrence of the organism in a lesion does not entitle it to be labeled one of the pure streptococcic dermatoses. To be fairly included in such a category, definite etiologic relationship must be established.

On the other hand, the presence of the streptococcus in a given case, even as an accessory, may be of greater practical importance than the question of its precise place in the nomenclature

For this reason, and for the purposes of this paper, no special stress will be placed on the question as to whether the streptococcus plays a dominant or a contributory part in the production of a given lesion.

The chief concern at this time is to consider not so much whether certain dermatoses are or are not of purely streptococcic origin as to review the reactions which seem to assume special characters because of the presence of the streptococcus.

At the outset Sabouraud's criteria of the presence of streptococci may be quoted: "Whenever an extensive area of skin oozes abundantly with a rosy, serous, limpid fluid; whenever one observes upon an eroded epidermal surface the presence of yellowish, unctuous, elevated or flat, but generally thin, papyraceous crusts, checkered with fissures, the presence of the streptococcus in the underlying lesion may be affirmed."

IMPETIGO CONTAGIOSA

The arch type of pure streptococcic dermatosis is impetigo contagiosa. The characteristic behavior of the skin invaded by streptococci may best be seen in this disease. While staphylococcic lesions tend to circumscription, streptococcic lesions tend to peripheral extension.

* Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

The exudate of streptococcic lesions is serous rather than purulent. The fibrinous exudate, which becomes apparent when the discharge diminishes, is also distinctive. It is thin, clear and whitish, or of a light, rosy hue.

The primary lesion of impetigo is a minute vesicle containing a clear, serous fluid. The corneous envelop is fragile and ruptures spontaneously or following slight trauma. An abundant effusion is at once in evidence and this quickly coagulates, forming the typical, yellowish crust. Beneath this crust the process continues; the surrounding corneous layer is elevated about the circumference, finally rupturing, whereupon a new and larger crust results.

While the streptococcus often evinces a selective preference for certain sites, such as the folds of the skin, this tendency is not noted in impetigo.

Just as impetigo may be regarded as a pure streptococcus infection of the epidermis so erysipelas may be considered with respect to the deeper tissues. The ordinary whitlow is generally considered as streptococcic in origin. Both of these conditions are on the borderline between surgery and dermatology.

A consideration of the purely dermatologic lesions in which the streptococcus plays a variable part is not only of interest but of importance from the standpoint of therapy. If we follow the French authors who have studied the question so minutely we shall deal with such topics as impetiginization, the distinction between impetigo, impetiginization and simple streptococcic infection, recurrent dermatoses from slumbering foci, the intertrigo group and various other consecutive reactions.

While many of these discussions may appear to be of only academic interest, their pursuit will tend rather to clarify than to confuse. A comparison of French and American textbooks leads inevitably to the conclusion that either French writers exaggerate or we minimize the importance of the subject.

IMPETIGINIZATION

One of the first questions to concern us is the application of the term impetiginization. As usually employed, this designates the characteristic symptoms of impetigo superimposed, no longer in isolated spots but diffusely, upon some preexistent dermatosis which, beneath the complication, retains its own individuality.

The essential difference between impetigo and impetiginization is that the former spreads by isolated foci while the latter spreads peripherally. When inoculated on an epidermis already open and deprived of its stratum corneum it can no longer form the characteristic vesicle, since the covering for it is wanting.

Some years ago the diagnosis of impetiginous eczema was frequently made. The picture conveyed by that term was roughly that of a crusted eczema. It retained a semblance of eczema but yielded to the treatment of impetigo.

Sabouraud has described and sought to make a definite entity of chronic streptococcic epidermitis. It occurs in three phases, the first of exudation, the second of prelichenoid impetiginization and the third of purely lichenoid aspect. In the end it presents dry, thickened patches covered with slightly scaly papules. At times it reverts to its exudative phase.

Darier considers this a chronic, microbic, lichenoid eczema. Neither Darier nor Brocq denies the presence of the streptococcus. The patches represent an appearance somewhat between that of chronic eczema and lichenification. Because they do not exhibit the pseudopapules of lichenification and because they show moisture at times, they are most often regarded as eczema, or eczema plus a microbic infection.

The question of infectious eczematoid dermatitis must be considered in this connection. Engman, who first described it, regards it as of staphylococcic origin but apparently includes in its category the condition formerly termed impetiginous eczema. Fordyce also includes under the same title many sharply defined dermatoses as well as lesions following ecthyma and intertrigo, all of which carry at least the suggestion of the streptococcus.

If the term is used in the comprehensive sense indicated by both of these writers it would seem to be descriptive of a group or better, perhaps, of a reaction rather than of a distinct entity. Moreover the cases recorded by each seem always to have been infectious at the outset and eczematoid only secondarily. This at once suggests the distinction that an infectious eczematoid dermatitis is an infection which has become eczematized, while an impetiginous eczema is an eczema which has become impetiginized.

I do not insist that the old impetiginous eczema was always primarily an eczema, but I do believe it incontestable that eczema often becomes secondarily infected with streptococci and that such cases present definite characters which are well described by the term impetiginization.

The case history presented herewith will be of interest:

REPORT OF CASE

L. D., a boy, aged 16 years, was vaccinated on the left arm six months ago. Infection supervened and healing was delayed. Crusted lesions developed about the wound, and subsequently another eruption appeared on the right thigh just above the knee. At the date of consultation both lesions were of several months' duration. The patch on the arm was obviously formed by the coalescence of a number of circular lesions. The surface was covered with a fine, fibrinous

exudate, with here and there a few crusts. It was apparently a frank case of impetigo. On the thigh was a circular area approximately 5 cm. in diameter, sharp in outline, markedly thickened and presenting some thin scales with a few exceedingly fine vesicles at the periphery. Aside from this last evidence the lesion was dry. The appearance was that of chronic streptococcic epidermitis of Sabouraud.

COMMENT

We find, then, in the same subject an uncomplicated impetigo and an infectious eczematoid dermatitis. Engman states that it is not unusual to find both conditions in the same person. If one grants the streptococcic origin of impetigo, it is difficult to eliminate the possibility of its influence in the consecutive eczematoid dermatitis.

It is true also that the form of infectious dermatitis so often observed following discharge from the nose, ears, sinuses, etc., in which the staphylococcus is the offending organism, may become eczematized.

From the evidence at hand it would seem difficult to consider infectious eczematoid dermatitis otherwise than in the light of an infection, either staphylococcic or streptococcic, eczematized. Furthermore, it would appear necessary to distinguish between it and an eczema, a dermatitis or any dermatosis which has secondarily become impetiginized. The distinction should rest on the character of the original eruption.

INTERTRIGO GROUP

Under the title "Chronic Sequelae of Acute Impetigo," Sabouraud has described a group of dermatoses which recur from time to time as the result of the activation of quiescent foci of streptococcic infection. This phase of the subject is intimately connected with the question of the intertrigo group.

Concerning intertrigo in general it may be noted that the marked predilection of the streptococcus for cutaneous folds is undeniable. Sabouraud maintains that all intertrigos are either primarily streptococcic or secondarily infected with the streptococcus. Often an intertrigo appears eczematous because of the fine vesicles it exhibits. These vesicles, however, are found at the periphery of the lesion. At the bottom of the fold will be found a fissure covered with the characteristic exudate and all such lesions will give within twelve hours a culture of streptococci.

The recurrent forms originate frequently in the retro-auricular fold. Behind the ear a yellowish, crusted lesion is observed. In pulling the ear forward to obtain a good view a fissure is opened. Two eroded surfaces are in apposition and their borders are covered with yellowish crusts. On removal of these crusts the underlying surface is seen to be covered with a fine, fibrinous exudate.

From such a chronic focus a process may extend directly, to involve considerable areas of the scalp, or the infection may be spread by the fingers, as in scratching. Until this more or less quiescent lesion is recognized and treated, recurrent attacks of impetigo may be the rule. The retro-auricular fold and the nostril are the two regions particularly prone to harbor these foci. Blepharitis is possibly of a like nature.

The term *ecthyma* has gradually come to mean an impetigo which, because of bad hygiene or anything lowering the resistance of the subject, has invaded the deeper tissues and caused *rupia*-like lesions which heal only with scar formation. Aside from their depth and indolence, they are not materially different from ordinary impetigo.

Likewise to be classified with chronic impetigo are the circumscribed forms of *pityriasis simplex* of the face, called by French authors "*dartres volantes*." These are seen chiefly in children, and in former times were regarded as evidence of a strumous diathesis. The lesions are circular or oval, superficial, well defined and covered with fine branny scales. While undoubtedly the streptococcus is the exciting cause, it is possible that the question of the soil is also to be carefully considered.

Another example of the preference of the streptococcus for the folds of the skin is *perlèche*. This infection attacks the labial commissures. The primary lesion is a fissure at the bottom of the fold which is somewhat eroded and on which the characteristic, fine, fibrinous exudate is seen. On each side of the fissure there is epidermal thickening. Cultures will give streptococci in a few hours.

SUMMARY

Each of the conditions we have discussed as streptococcic dermatoses presents a definite clinical picture.

Impetigo, *ecthyma*, *intertrigo* and *perlèche* are matters of such common agreement that no comment is needed.

Impetiginization is a diffuse form of impetigo secondarily affecting an antecedent dermatosis which retains its own individuality.

Infectious eczematoid dermatitis denotes the eczematization of an infection, the infection preserving its own character in spite of the complication.

Chronic forms of impetigo are frequent. They present such lesions as circumscribed plaques of *pityriasis*, as well as impetiginous processes behind the ears, on the scalp and about the nose and eyes.

The character of the soil and certain internal influences may account for some objective differences in lesions due primarily to streptococci.

What seems probably the determining factor of most importance is the variation in the organism itself.

Unna has maintained that different strains of streptococci may one day be demonstrated in the production of the various forms of impetigo. Certainly it will not appear far fetched to reason that, just as different strains of streptococci have been isolated in scarlatina, erysipelas and measles, so they may be isolated in impetigo, ecthyma, intertrigo and other dermatoses.

391 Sutter Street.

ABSTRACT OF DISCUSSION

DR. AUGUST RAVOGLI, Cincinnati: I cannot agree with Dr. Chipman as to eczematoid dermatitis. Eczema is a dermatitis. Dermatitis is not an eczema, consequently the blending of the term "eczematoid dermatitis" is not very clear to me. That the streptococcus is the cause of a great many infections of the skin there is no doubt, as, for instance, the impetigo seen so often in children. Another disease caused by the streptococcus which Dr. Chipman did not mention is *panaritium superficiale bullosum* tourniole of Sabouraud, an infectious inflammation of the epidermis. It is a kind of bulla formation around the third phalanx of the finger and around the nail, containing purulent serum. I have seen a child infected with the streptococcus and in consequence thereof develop a dermatitis exfoliativa, the whole body being covered with the bullae. The nurses often develop a streptococcic infection from attending these patients. The question between eczema and kindred affections consists in the quality of the pus cocci. If it is staphylococcus or streptococcus, if the coccus is yellow, or of the Bockart variety that produces sycosis, all are capable of producing practically the same affection, only in different degree. The streptococcus in the skin is capable of producing some general affection and reaction in the system. The trichophyton fungus which vegetates superficially on the epidermis is capable of producing a general reaction and antibodies are formed. The streptococcus is capable of producing a lymphangitis and affecting the lymph vessels and causing cutaneous abscess.

DR. CHARLES J. WHITE, Boston: As to the differential diagnosis between the epidermophyton and streptococcic infections, it is often difficult to determine which disease is present. Those who have not worked with the epidermophyton may think it is simple to make cultures and demonstrate the plant, but such an idea is far from the truth. As Dr. Chipman has said, the streptococcic infections seem to spread peripherally. That is not what the epidermophyton does. It comes up as a vesicle and remains in that form. Another point is that the streptococcic lesions are larger than those produced by the epidermophyton.

DR. DOUGLASS W. MONTGOMERY, San Francisco: Much of the advancement of our knowledge is due to French observers, particularly to Gougerot, who while at the front became acquainted not alone with streptococcic infections of the skin, but also with them as a disease of wounds. The Rockefeller Institute has also done much in differentiating the different strains of streptococci. The streptococci have several broad, general characteristics; one of them is their fondness for moisture. They like to dwell in moist places such as the folds of the skin, and, having infected the skin, they attract a vast quantity of serum to the infected area. It is now well known that the ordinary ulcer of the leg is a

streptococcic infection, and it is probable that the reason for the continuance of the infection in this situation is the unusual moisture of the tissues, due to venous stasis. Another broad characteristic of the streptococcus, determining its clinical behavior, is its anaerobic nature. A man will receive a wound, for instance, which becomes streptococcically infected, and the wound will heal. But it heals with colonies of viable streptococci inclosed in the tissue. Afterward, as so often happened in the war, a secondary operation for relief of a deformity is performed, which may be done with faultless aseptic technic. Nevertheless, a streptococcic infection takes place, emanating, not from the outside, but from the streptococci still resident in the tissues.

DR. FRANK C. KNOWLES, Philadelphia: While serving with the British forces in France I had an opportunity of seeing many forms of impetigo. McCormick, a well-known British dermatologist, who was at the front over four years carrying out a series of experiments to determine the nature of the offending streptococcus, found *Streptococcus faecalis* to be responsible in most cases. On returning home it occurred to me that a further study might prove interesting. Thirty cases were studied and of these twenty-eight were of the hemolytic strain. Unfortunately, five strains were discovered, but only one of the *S. faecalis* type.

DR. CHARLES M. WILLIAMS, New York: The streptococci tend to form groups, surrounded by normal skin, whereas the ringworm infections are apt to be scattered here and there, not forming such distinct outlines. The second point is the frequent occurrence of such forms of pyoderma with infections of the nose. It is a common concomitant of catarrh. Frequently a report will come from the nose specialist stating that it is a simple rhinitis and does not amount to anything, but until you get some competent rhinologist to cure the rhinitis no treatment of the skin will result in cure.

DR. RICHARD L. SUTTON, Kansas City, Mo.: I believe that the staphylococcus is probably the most frequent cause of the disease as seen in this country, particularly in the Middle West. The streptococcus may be a secondary invader, or, as in the cases reported by Dr. Chipman and by Dr. Knowles and his associates, it may be the sole invader in some instances. In the cases of infectious eczematoid dermatitis studied by Engman, by Fordyce and by myself, *Staphylococcus aureus* was also the offending agent. A thought suggested by Dr. White is important: In many instances tinea infection may simulate other disorders, dermatitis repens, for example. It is an easy matter to recover the ubiquitous staphylococcus, but isolation of the ringworm fungus is often a difficult process; consequently, it may be that we blame the staphylococcus for many lesions that should be credited to its yeastlike cousin. Some years ago Dr. Howard Morrow called attention to the fact that silver nitrate was almost a specific in the treatment of impetigo, and I wish to commend it very highly to you. It is employed in aqueous solution, 10 per cent., and if the patient does not object to the discoloration, it is one of the most valuable agents in the treatment of this condition.

DR. ERNEST DWIGHT CHIPMAN, San Francisco: I anticipated opposition to the views expressed concerning infectious eczematoid dermatitis. Dr. Sutton has defended the staphylococcus. There seems room for an honest difference of opinion on this score which time will probably settle to the satisfaction of all. Dr. Ravogli mentions the omission of the French tourniole from my list. I believe the term whitlow, which I touched on lightly, is the equivalent. Dr.

White properly emphasized the resemblance between some streptococcic lesions and the reactions due to the epidermophyton. In Dr. Engman's article, published nearly twenty years ago, on the subject of infectious eczematoid conditions, there appeared an illustration and description of a case which I believe he and all of us would unhesitatingly diagnose today as epidermophyton infection. It is probable that in the future we shall have a very much more specialized knowledge of the different strains of the streptococcus, not only those involving the deeper tissues but those which confine their activities more strictly to the epidermis.

Abstracts from Current Literature

THE PREVENTION OF SKIN TROUBLES FROM CUTTING OILS AND EMULSIONS. REPORT OF THE NATIONAL SAFETY COUNCIL, CHICAGO, No. 44, 1921.

Workers in cutting oils and emulsions frequently develop, on the exposed parts, black follicular plugs which often become secondarily infected, or vesicular eruptions or vegetating tumors. Persons with excessively hairy or dry skins are predisposed.

Most oils as received from the manufacturer are sterile; those made from crudes containing little or no paraffin and which have been highly refined are the most favorable. Excessive amounts of hydrocarbon sulphonates and fatty acids are undesirable. Used, unfiltered oils containing bacteria from workers' sputums and hands, and metal chips are particularly irritating.

Prophylaxis is obtainable in most cases by rigid hygienic practices. The parts should be scrubbed thoroughly at least twice daily in hot running water with liquid or powdered soap and a soft brush. If oil or a mixture of green soap and sawdust is used for cleansing, each workman should have an individual supply. The application of hydrous wool fat (lanolin) after washing will prevent chapping. Cleanliness of clothing and machinery, gloves, oil-cloth armlets, and the prompt and proper treatment of small cuts will impede the development of many infections.

It is useless to try to prevent skin troubles among some men who show extreme susceptibility to the irritating action of cutting oils. Such men should be transferred to other work where they will not be brought into contact with such oils.

Intracutaneous sensitization tests with oils during the course of the disease have not proved of much practical value, as negative results are frequent and immunization is not feasible. Injections of nonspecific proteins do not seem to immunize. In infected cases, autogenous and stock vaccines are of slight value. Fractional doses of roentgen rays are frequently very helpful. When the eruption is a dermatitis venenata, the itching is greatly relieved by one or two fractional doses, and when the eruption is a pustular folliculitis, a furunculosis or an infectious eczematoid dermatitis, involution often results after a few fractional doses at weekly intervals, accompanied by wet dressings of Burows' solution and vaccines. Ultraviolet rays from the Kromayer or Alpine lamps are also effective. In mild infections calamine lotion is soothing. Stimulating or irritating local remedies or ultraviolet rays are not permissible during roentgen-ray treatment, as they greatly enhance the action of the roentgen rays and may lead to severe local reactions.

(The following references may be of interest:

White, R. P.: *Occupational Affections of the Skin*, New York, P. B. Hoeber, 1920, p. 144.

Shie, M. D.: *Wound Infection Among Lathe Workers*, J. A. M. A. **69**: 1927, 1917.)

ANDREWS, New York.

DRACONTIASIS IN ANIMALS: WITH NOTES ON A CASE OF GUINEA-WORM IN A COBRA. D. A. TURKHUDD. Indian J. M. Res. 7:727 (April) 1920.

Turkhudd gives a complete summary of the literature on dracontiasis in animals and reports a case occurring in a cobra (*Naja tribudiens*). After the cobra had been in captivity in the laboratory for seven months and while venom was being extracted from it, a loop of worm about 1 mm. thick was noticed to be protruding from a slight swelling on the head. When the worm was examined under a microscope a central uterine tube containing active embryos was noted. These embryos were somewhat smaller than those of the human guinea-worm, but otherwise resembled it closely.

The snake was killed under chloroform and the worm was dissected out commencing at the opening in the swelling. The worm was found lying between the muscles on the back parallel to and along the right side of the spine. With the anterior portion missing, the worm was found to measure 12 cm. in length, ending in a short curved tail. The worm was 1 mm. in breadth, but in all respects resembled the human guinea-worm.

Some whitish fluid was taken from the opening on the head prior to the dissection. This fluid was found to be full of living embryos, somewhat smaller than those of the human guinea-worm, but otherwise resembling these in every respect. Cyclops were then added to the water containing these embryos, and on examination twenty-four hours later, out of twelve cyclops, ten or 83 per cent. showed infection. Fourteen days later, 150 infected cyclops were fed to six healthy cobras, so that each cobra received twenty-five infected cyclops. As a control three healthy cobras were similarly fed, each with twenty-five cyclops infected with embryos of the human guinea-worm. All the cobras died within the subsequent twelve months, but only two showed abnormal postmortem appearances. The first cobra died two and a half months after being fed with cyclops infected with embryos of the cobra guinea-worm. A worm about 3 cm. long and 1 mm. in thickness was found subcutaneously just under the abdominal scales. The second cobra died ten months after it was fed with cyclops infected with embryos of the human guinea-worm. Five worms were found within.

GUTIERREZ, Manila.

CONCERNING THE VIRULENCE OF SPIROCHETES FROM THE SITE OF INFECTION AFTER TREATMENT. FURTHER CONTRIBUTION TO EXPERIMENTAL RABBIT SYPHILIS. L. ARZT and W. KERL, Dermat. Ztschr. 32:326 (April) 1921.

Three remarkable experiments are cited by the authors. Two patients who had had syphilis and had received sufficient treatment to render them negative serologically presented themselves with erosions at the site of infection. These lesions regressed with no treatment. Examination of serum from the lesions did not reveal any spirochetes, yet inoculations into rabbits were successful. The rabbits developed generalized syphilitic lesions. A third patient had the scar of his lesion surgically removed. He had received treatment with arsphenamin and mercury rubs. The Wassermann reaction was negative. Spirochetes were demonstrated by the dark field and in sections from the scar. Rabbits inoculated with material from this scar developed generalized syphilis, which was transmitted through several passages. When the patient was examined after eight years without treatment, he was found clinically, sero-

logically and neurologically, including all tests on fluid, negative. The first two patients were always negative clinically with no treatment. These experiments are especially significant in relation to the problem of latency. If spirochetes were present in the scars and sites of primary lesions, other foci would have formed during the interval that the patients were without treatment from the period of the beginning of the experiment to the time of reexamination, in one case, eight years later.

GOODMAN, New York.

THE IMPORTANCE OF RECOGNIZING AND TREATING NEUROSYPHILIS IN THE EARLY PERIOD OF THE INFECTION. J. A. FORDYCE, *Am. J. Med. Sc.* **161**:313 (March) 1921.

A strong plea is made for a spinal fluid test of syphilitic patients before pronouncing them cured. Syphilis of the central nervous system begins probably in the first year of the infection, and in the writer's experience the number of cases corresponds roughly to the number of cases of late neurosyphilis. There is, however, no serologic evidence to show that the spinal fluid is normal in the early stage but becomes infected later.

The importance of spinal fluid examinations is evidenced by the fact that neurosyphilis may be plainly evident, very slight or may present no symptoms at all, and that the usual routine treatment is seldom sufficient to cure the disease, when such involvement has occurred. In fact, symptoms indicating neurosyphilis may be manifest during or shortly after arsphenamin and mercury treatment and call for further treatment, together with intraspinal medication. Experience has shown that the early neurosyphilitic patients can be cured more rapidly, and in the majority of cases cured only by combined intravenous and intraspinal methods. Preference is given to the Swift-Ellis method over reinforcement with minute quantities of arsphenamin.

Patients having a negative spinal fluid with all other tests negative after a thorough and sufficiently prolonged course of treatment can be reasonably assured of future immunity.

JAMIESON, Detroit.

A CONTRIBUTION TO THE STUDY OF CHRONIC ATROPHIC DERMATITIS (ERYTHROMELIE OF PICK; ACRODERMATITIS CHRONICA ATROPHICANS OF HERXHEIMER). PAUTRIER and O. ELIASCHEFF, *Ann. de dermat. et syph.* **6**:241, 1921.

A typical case of this affection is described, occurring in an otherwise healthy farmer of 38 years. Both lower extremities were involved, the left especially, the lesions being of twenty-two years' duration, and the only subjective symptom being a slight chilling sensation. A biopsy examination was made and is described in detail, its most peculiar feature being a proliferation of the walls of the blood vessels, superficial and deep, resulting in partial occlusion of their lumens. The inflammatory element in the picture is stressed in the discussion, and the authors object to the condition being classed as an idiopathic atrophy.

More commonly found in the colder regions of central Europe, it is suggested that cold may be an etiologic factor, but as these regions also show a prevalence of goiter, the authors believe that thyroid gland disorders may be causative, as is thought to be true of scleroderma. Further observations are needed.

PARKHURST, New York.

EXPERIMENTAL SYPHILIS IN THE RABBIT. VI. AFFECTIONS OF THE BONE, CARTILAGE, TENDONS AND SYNOVIAL MEMBRANES. Part 1. Lesions of the Skeletal System, Part 2. Clinical Aspects of Syphilis of the Skeletal System, Affections of the Cranial Bones and Bones of the Forearm. Part 3. Syphilis of the Posterior Extremities with Other Affections of a Miscellaneous Type. WADE H. BROWN, LOUISE PEARCE and W. D. WITHERBEE, J. Exper. Med. **33**:495 (April) 1921.

Localized infection of bones and tendons was found frequently, especially on the face, feet and legs, most of the lesions arising from the periosteum but also developing from within the bone marrow cavities or epiphyseal lines. Periosteal lesions were either localized masses or were diffuse, showing histologically the typical syphilitic granulomas. Absorption and necrosis of bone were accompaniments of periosteal lesions and were found especially in the facial bones and bones of the feet. Bone lesions were essentially the same as periosteal lesions, but those arising from the marrow cavities were composed chiefly of polyblastic infiltrations.

Lesions of tendons or tendon sheaths were occasionally seen.

The clinical history disclosed the fact that the bone lesions were among the earliest of the generalized forms of the disease, pursued a comparatively rapid course and had no relapse. It was also found that an analogy exists between certain forms of the animal and human affections, this being pronounced in the nasal and epiphyseal lesions in the rabbit compared with congenital syphilis in man. Induced syphilis of the osseous system is capable of being favored or inhibited, according to the experimental conditions employed. Many infections were found which were not accompanied by distinctive signs sufficient to indicate their existence, which might also be analogous to the infections in man when latency exists.

JAMIESON, Detroit.

STUDIES ON X-RAY EFFECTS. VI. EFFECT OF THE CELLULAR REACTION INDUCED BY X-RAYS ON CANCER GRAFTS. J. B. MURPHY, R. G. HUSSEY, W. NAKAHARA and E. STURM, J. Exper. Med. **33**:299 (March) 1921.

An erythema dose of roentgen rays was given on small areas of the groin of mice, and a week later these irradiated areas and also those areas which were not irradiated in the groin opposite were inoculated intracutaneously with a graft of cancer. The irradiated areas showed a low percentage of takes, the protected areas the usual normal amount. If the grafts were introduced subcutaneously they grew equally well in both areas. This could be explained by the histologic examination which showed that a few days after irradiating the skin layers only were markedly infiltrated with round lymphoid cells, this infiltration possibly controlling the grafts made into but not under the skin.

STUDIES ON X-RAY EFFECTS. VII. EFFECT OF SMALL DOSES OF X-RAYS OF LOW PENETRATION ON THE RESISTANCE OF MICE TO TRANSPLANTED CANCER. W. NAKAHARA and J. B. MURPHY, J. Exper. Med. **33**:429 (April) 1921.

After treating mice with small doses of roentgen rays which were capable of producing a lymphoid stimulation, a relatively increased resistance was found to a certain type of transplantable cancer. This increased resistance could be determined in from three to seven days after treatment.

STUDIES ON X-RAY EFFECTS. VIII. INFLUENCE OF CANCER INOCULATION ON THE LYMPHOID STIMULATION INDUCED BY SMALL DOSES OF X-RAYS. W. NAKAHARA and J. B. MURPHY, *J. Exper. Med.* **33**:433 (April) 1921.

A suppression of lymphoid stimulation occurs if cancer inoculation is performed immediately after exposure to roentgen rays, but if inoculation is delayed for seven days, a second stimulation occurs in a larger proportion of mice so treated. In those treated by the latter method the state of resistance is attended by blood lymphocytosis.

JAMIESON, Detroit.

EXPERIMENTAL MEASLES. F. G. BLAKE and J. D. TRASK, JR., *J. A. M. A.* **77**:192 (July 16) 1921.

Experimental investigation of the disease in monkeys was conducted for the purpose of devising a method of preventive inoculation. It was found that monkeys are susceptible to the disease, which confirms the contention of Anderson and Goldberger.

Transmission of the disease from monkey to monkey for many generations is readily accomplished by the use of nasopharyngeal washings, citrated and defibrinated whole blood, serum injected subcutaneously, intravenously, and intratracheally, and by intimate contact infection. One attack of experimental measles confers immunity against reinfection.

Blake and Trask found that passage of infection from monkey to monkey by injection of large amounts of blood led to diminution of virulence, thus disappointing their expectation of obtaining a potent "fixed" virus. They determined, however, that the attenuated virus obtained in this way caused a reaction when injected intracutaneously. Their experiments have not reached the stage where it can be said that such local injection consistently causes the development of an active immunity, though in certain instances the development of an effective immunity is indicated.

MICHAEL, Houston, Texas.

STUDIES ON MEASLES. I. SUSCEPTIBILITY OF MONKEYS TO THE VIRUS OF MEASLES. II. SYMPTOMATOLOGY AND PATHOLOGY IN MONKEYS EXPERIMENTALLY INFECTED. H. G. BLAKE and J. D. TRASK, JR., *J. Exper. Med.* **33**:385 (March) 1921.

It was found that monkeys are susceptible of inoculation with the virus of measles. This was done by intratracheal injection of filtered and unfiltered nasopharyngeal washings of patients with measles, and a relatively constant group of symptoms was induced which closely resembled measles in man.

The symptoms and course of the disease closely parallel those in man, and the microscopic pathology of the skin and mucous membrane lesions are practically identical with the corresponding human lesions.

JAMIESON, Detroit.

STUDIES ON MEASLES. III. ACQUIRED IMMUNITY FOLLOWING EXPERIMENTAL MEASLES. F. G. BLAKE and J. D. TRASK, JR., *J. Exper. Med.* **33**:621 (May) 1921.

This work shows that the effect of measles in monkeys is the same as in man, one attack producing immunity to reinfection. The result is the same whether heterologous or homologous virus is used or whether intravenous or mucous membrane inoculation is used.

JAMIESON, Detroit.

MULTIPLE CARCINOMA OF THE SKIN: "PRECANCEROUS DERMATOSIS OF BOWEN." J. H. SEQUEIRA, Brit. J. Dermat. & Syph. **33**: 173 (May) 1921.

Sequeira describes a case of precancerous dermatosis of Bowen occurring in a woman who was 57 years of age when first seen in 1912. At that time she had several tumor lesions on the forehead, which disappeared following radium treatment. She returned in 1920 presenting lesions on the left arm, right thigh, back, the front of the trunk and right knee, while the forehead showed a broad crescentic area of scarring, with a few palpable, pinhead sized, slightly raised thickenings. The lesion on the left arm, which appeared as a nodular irregularly-shaped excrescence, had been present for four months, while that on the right thigh was a button-like skin tumor with a broad base, rounded edge and granular surface. The growths on the back, which appeared in 1912, varied from small tumors to large excrescences, two of the patches looking not unlike those of Paget's disease.

The article, which is to be continued, also contains a résumé of the cases reported by Bowen and Darier.

SENEAR, Chicago.

SUPERINFECTION IN EXPERIMENTAL SYPHILIS FOLLOWING THE ADMINISTRATION OF SUBCURATIVE DOSES OF ARSPHENAMIN OR NEO-ARSPHENAMIN. WADE H. BROWN and LOUISE PEARCE, J. Exper. Med. **33**:553 (May) 1921.

Animals used in these experiments were inoculated and reinoculated with a virus of essentially the same virulence and eighteen days later were treated with original arsphenamin and neo-arsphenamin (6 mg. and 9 mg. per kilo, respectively). This dose was chosen for the purpose of producing definite regression of lesions with a relapse two or three months later. Five days after treatment these animals and untreated controls were reinoculated with the same original virus. Relapses occurred in all treated but not reinoculated patients, showing that the dose was subcurative. In the reinoculation of infected controls the majority of lesions were of a nonspecific inflammatory type, possibly a slight local infection. On the other hand, all but two of the reinoculated treated animals developed typical chancres, in most instances the second chancre overgrowing recurrence of the original lesions.

They conclude that in animals the presence of *Spirochæta pallida* does not prevent the possibility of a second infection with the same organism. As this state may be induced experimentally by treatment with arsphenamin or neo-arsphenamin, insufficiently treated or uncured patients may be rendered as susceptible to a second infection as a normal person, the manifestations being indistinguishable from those of the original infection.

JAMIESON, Detroit.

EPITHELIOMA OF THE HAND WITH A TENDENCY TO SPONTANEOUS CURE. C. E. CORLETTE and KEITH INGLIS, M. J. Australia **1**:250 (March) 1921.

The case reported is that of a man 63 years old, suffering from a lesion of nine months' duration. This lesion started as a small sore on the dorsum of the left hand near the metacarpophalangeal joint of the middle finger. The

sore being treated, healed, leaving a ridge at the margin. This ridge continued to advance, the center healing as the periphery advanced. At the time of examination the lesion was found spreading from the base of the thumb across the hand, just below the wrist joint and ending near the base of the ring finger where it was rough, irregular and almost horny. The lesion was not attached to the deeper structures. There was no glandular enlargement. The center appeared to be healed scar tissue. The Wassermann reaction was negative at two different times. Microscopic examinations of serum from the lesion was negative for spirochetes in the dark field. Examination for bacteria or other parasites was negative. Histologic sections both before and after operation were those of epithelioma. The patient made a complete recovery.

GUTIERREZ, Manila.

STUDIES IN FAMILIAL NEUROSYPHILIS. I. CONJUGAL NEUROSYPHILIS. J. E. MOORE and A. KEIDEL, J. A. M. A. **77**:1 (July 2) 1921.

Fifty-two partners of fifty neurosyphilitic patients were examined by these investigators. The examination included a careful anamnesis, physical and neurologic study, a Wassermann reaction of the blood, and cell count, globulin, Wassermann and colloidal tests of the cerebrospinal fluid. Of the whole number of fifty-two partners, forty were syphilitic, and of these, twenty-one had neurosyphilis. Of the twenty-one instances of neurosyphilis, the type was similar in both partners eight times; three couples had paresis, two had tabes, and three cerebrospinal syphilis of the same type.

The authors obtained a higher percentage of conjugal neurosyphilis than previous investigators, but this is attributed to the routine investigation of the spinal fluid. Routine examination of the partners of neurosyphilitics is of practical value. That spinal fluid examination is an indispensable part of the routine is indicated by the discovery of asymptomatic neurosyphilis in seven partners.

The authors feel that their study does not justify any decision as to the duality of spirochetal strains.

MICHAEL, Houston, Texas.

SILVER-ARSPHENAMIN. ESCHER, *Ann. de dermat. et syph.* **5**:203 and **6**:257, 1921.

In an exhaustive manner, with a bibliography including fifty-two articles, the author considers the chemical structure, physical and chemical properties, dosage and curative power of the new arsenical. Much of the material for this article was secured from the Medical Corps of the American Expeditionary Forces in Germany, and has already been incorporated in a similar paper, with a similar bibliography, by Walson (*Silver-Salvarsan in the Treatment of Syphilis*, *Am. J. Med. Sc.* **3**:418, 1921). Unlike Walson, however, Escher mentions the frequency with which icterus has followed this new medication in the hands of some workers. He also relates three cases of fatality which he has found in the literature, hemorrhagic encephalitis having been the terminal event in three and pneumonia following a generalized dermatitis in the fourth.

Escher concludes that in silver-arsphenamin we have a valuable new drug, whose toxicity is lower than that of arsphenamin, and whose therapeutic powers at least equal those of arsphenamin and surpass those of neo-arsphenamin.

min, sodium-arsphenamin and arsphenamin-sulphoxylate. In neurosyphilis the results of its use are said to be excellent, but the author advises against undue enthusiasm until time and careful observation have proved this.

PARKHURST, New York.

TWO CASES OF CONGENITAL ACANTHOSIS NIGRICANS WITH DIABETES MELLITUS. GUIDO MIESCHER, *Dermat. Ztschr.* **32**:276 (April) 1921.

A unique instance of familial acanthosis nigricans is reported. Two children, a boy and a girl, presented since birth lesions of the skin characteristic of the disease. The father presented nevroid lesions which were histologically indistinguishable from acanthosis nigricans. In addition to the skin lesions, the children were not normal in other respects. They both had diabetes mellitus. The mental development was retarded, and they were distinctly imbecile. Lanugo hairs were profuse. The girl had not yet begun to menstruate, although 19 years of age. The boy also had a condition of the scalp considered cutis verticis gyrata. The question of etiology and the distinction between benign and malignant cases of the disease are discussed. It seems inappropriate to classify cases as benign and malignant because the adjective can only refer to the underlying cause, as for example, carcinoma. Those instances of the disease which are congenital, and the number is growing, cannot depend on such etiology, and cases such as the two presented lend credence to the idea that some disturbance of glands of internal secretion which have to do with the development of the skin is the underlying cause in such cases.

GOODMAN, New York.

STUDIES ON DECREASING THE REACTION OF NORMAL SKIN TO DESTRUCTIVE DOSES OF X-RAYS BY PHARMACOLOGICAL MEANS AND ON THE MECHANISM INVOLVED. J. AUER and W. D. WITHERBEE, *J. Exper. Med.* **33**:791 (June) 1921.

Using four groups of rabbits, roentgen-ray treatment of 30 skin units was administered on the ears of the rabbits. Normal rabbits composed the first group; rabbits injected intraperitoneally with 10 c.c. of horse serum thirteen days after roentgen-ray treatment formed the second group; the third group was composed of rabbits treated by two subcutaneous and two intramuscular injections of 1 c.c. of horse serum each at three to four day intervals followed in ten days by roentgen-ray treatment; the fourth group was made up of rabbits prepared as Group 3 but reinjected with 10 c.c. of horse serum thirteen days after treatment.

It was found that the usual changes followed by local gangrene developed in the normal rabbits in about thirty-three days; in the second group in from thirty-six to fifty days; in the fourth or sensitized reinjected group in from fifty to eighty-five days; but in the sensitized animals of Group 3 the results appeared in from forty-six days (one animal) to no gangrene even after 340 days.

This remarkable immunity to lethal doses of roentgen rays is explained on the assumption that in the sensitized animals there are still anaphylactic bodies present bound to the cells of the treated area, these bodies disappearing following the injection of serum after the roentgen-ray treatment.

JAMIESON, Detroit.

TWO NEW CASES SHOWING THE COINCIDENCE OF NERVOUS AND NON-NERVOUS MANIFESTATIONS IN A SYPHILITIC PERSON. SIMON, Bull. Soc. franç. de dermat. et syph. **5**:165, 1921.

In a man, aged 25 years, who presented supposedly tertiary syphilitic involvement of the penis and inguinal lymph nodes, both Achilles reflexes were absent. The spinal fluid findings were negative.

A man, aged 33 years, presented a costal osteoperiostitis and a facial paralysis. Nothing is said of the spinal fluid. It is not unlikely that the paralysis was due to the pressure of a periostitis in the fallopian canal.

Neither case seems conclusive, but they were presented to stimulate discussion regarding spirochetal strains. Queyrat suggests that in each case of early syphilis the exact morphology of the spirochetes be noted and kept in mind as the progress of the case is observed; it is possible that a certain type may be found to cause lesions of the nervous system.

PARKHURST, New York.

PARESIS TREATMENT BY ARSPHENAMIN AND MERCURY. C. A. BONNER, Boston M. & S. J. **185**:60 (July 14) 1921.

This article contains a rather general discussion of the treatment of paresis by the intravenous injection of arsphenamin in a series of cases treated at the Warren State Hospital, Pennsylvania. Results at the end of two years are given.

LANE, Boston.

THE A B C OF RADIUM. ERNEST M. DELAND, Boston M. & S. J. **184**:696 (June 30) 1921.

This article contains a discussion of the physics of radium, the technic of radium therapy, the methods used at the Huntington Memorial Hospital, Boston, the effects on tissue, and general indications for radium treatment, both superficial and deep.

LANE, Boston.

EFFECT OF SMALL DOSES OF X-RAYS ON HYPERTROPHIED TONSILS AND OTHER LYMPHOID STRUCTURES OF THE NASOPHARYNX. J. B. MURPHY, W. D. WITHERBEE, S. L. CRAIG, R. G. HUSSEY and E. STURM, J. Exper. Med. **33**:815 (June) 1921.

Using a dose of roentgen rays equivalent to from 1 to 1¼ skin units (filtered through 3 mm. of aluminum), the writers state that atrophy of the tonsils and adjacent lymphoid structures can be accomplished. An area about 3 inches square under the angle of the jaw on each side is exposed with this dose, which is repeated in a few weeks if necessary. The degree of atrophy can be determined by experience, and such treatment does not prevent surgical removal if sufficient reduction does not follow. In all but three or four cases one treatment was sufficient, improvement probably following improved drainage resulting from atrophy of the lymphoid tissue.

JAMIESON, Detroit.

DARIER'S DISEASE. HUDELO, BIGOT and CAILLAU, Bull. Soc. franç. de dermat. et syph. **5**:159, 1921.

A boy, 16 years of age, presented keratotic lesions on the forehead, behind the ears, about the jaws, along the nasolabial folds and beneath the clavicles.

The microscope confirmed the diagnosis of follicular dyskeratosis, some of the lesions, however, being nonfollicular.

It is of interest to note that this patient had first appeared, in July, 1920, with an eczema of the scalp and face and a pronounced keratosis pilaris of the extremities. There was then no sign of Darier's disease, which appeared later while tar preparations were being used to combat the eczema.

Darier recommends polyglandular endocrine treatment.

PARKHURST, New York.

ANTIVENEREAL PROPHYLACTICS; RELIABILITY AND EFFECT.

J. SCHUMACHER, *Deutsch. med. Wchnschr.* **47**:626 (June) 1921.

The author recommends a 1:1,000 solution of mercuric chlorid as the most effective antisyphilitic prophylactic. The penis should be well bathed, especially the fossa navicularis. The widespread calomel ointment has no reliable disinfecting power at all—as it is nonsoluble and lacks free mercury ions which alone guarantee disinfection. For gonorrhea a 1 per cent. solution of albargin proved most effective. The penis should be well bathed in this solution—injection is not necessary—but a match mounted with wadding well soaked in albargin should be used for wiping out the fossa navicularis.

AHLWEDE, Hamburg.

A NEO-ARSPHENAMIN FATALITY. NICOLAS and J. LACASSAGNE, *Ann. de dermat. et syph.* **6**:280, 1921.

A strong Italian girl of 20 years, under treatment for a secondary papulo-squamous syphilitic eruption, had received an initial injection of 0.3 gm. of neo-arsphenamin; a week later a second injection, amounting to 0.45 gm. was given. A large ampule was used, containing 0.9 gm., the distilled water being placed in the ampule to dissolve the powder; the remaining 0.45 gm. was administered to another patient. Two days later the girl developed nervous symptoms, with respiratory disturbance, coma and convulsions, death ensuing within twenty-four hours. The other patient experienced no reaction; therefore this fatality seems to be due to a reaction of the individual, and not to any toxicity of the neo-arsphenamin.

PARKHURST, New York.

DOSAGE OF ARSPHENAMIN. K. BIELE, *Deutsch. med. Wchnschr.* **47**:619 (June) 1921.

A woman of 26 was given 3 gm. of neo-arsphenamin in one injection by mistake instead of 0.3 gm. Previously she had received 0.45 gm. of neo-arsphenamin and had undergone a two course treatment with mercury. The patient showed slight symptoms of intoxication until the fifth day after injection and then fully recovered. The Wassermann reaction was still positive one week after the injection; it turned negative, however, without further treatment five weeks later.

AHLWEDE, Hamburg.

MACULAR ATROPHY OF THE SKIN. HUDELO and WALTER, *Bull. Soc. franç. de dermat. et syph.* **5**:162, 1921.

A girl, 21 years of age, had noticed unusual redness of the cheeks and chin eight months previously. At present there was a palm-sized patch on the thorax, made up of pallid, atrophic macules on a reddish background that

was slightly squamous. The face and the lumbar spine showed similar macules, much less marked. There were no subjective symptoms; the sensations were not disturbed.

Several diagnoses were considered, including atrophic lichen planus, white spot disease, Jadassohn's anetoderma and atypical parapsoriasis, but a biopsy examination was thought to be the only means of settling the question. To further complicate the picture, an atrophic spot was found on the palate.

PARKHURST, New York.

STUDIES ON LYMPHOID ACTIVITY. V. RELATION BETWEEN THE TIME AND EXTENT OF LYMPHOID STIMULATION INDUCED BY PHYSICAL AGENTS AND THE DEGREE OF RESISTANCE TO CANCER IN MICE. J. B. MURPHY, W. NAKAHARA and E. STURM, *J. Exper. Med.* **33**:423 (April) 1921.

Heat or small doses of roentgen rays are capable of stimulating lymphoid tissue to greater resistance to transplanted cancer. The former is sluggish at first, then latent, and is later more pronounced; the latter produces a sharp depression followed by a marked stimulation lasting a longer time. Inoculation of cancer at the height of the stimulation phase shows marked resistance with both roentgen rays and heat.

JAMIESON, Detroit.

LUPUS VULGARIS OF THE FACE WITH NASAL HYPERTROPHY SIMULATING RHINOPHYMA. G. THIBIERGE and RABUT, *Bull. Soc. franç. de dermat. et syph.* **5**:176, 921.

A woman, aged 58 years, since 1910 had had lupus vulgaris of the cheeks, which had been cauterized. In 1916 her nose became dusky red, large and crusted, showing nodules. When shown, the lesions of the cheeks were again active, and the tip of the nose, measuring 5 cm. in its transverse diameter, was violaceous, smooth and soft, with no nodules but many superficial scars. There was no tendency to destruction of the part. The cervical lymph nodes were palpable. The nasal enlargement was attributed to a chronic lymphangitis, such as often affects the lip.

Darier advises a biopsy and animal inoculations to verify the diagnosis.

PARKHURST, New York.

INVESTIGATION OF LIVER FUNCTION IN SYPHILITICS, WITH ESPECIAL REFERENCE TO ICTERUS SYPHILITICUS PRAECOX AND ARSPHENAMIN LIVER DISTURBANCES. PAUL TACHAU, *Dermat. Ztschr.* **32**:305 (April) 1921.

The author sought to get an idea of the liver function in icterus syphiliticus praecox by blood chemistry studies. There is a definite derangement of carbohydrates. From this it seems that Buschke was right in claiming a damage of the liver parenchyma through spirochete toxins. No pathologic blood chemical findings, as far as carbohydrate was concerned, could be determined for congenital syphilitic infants. Although the few cases studied of liver function among syphilitic patients treated with combinations of mercury and arspenamin do not warrant conclusions, Tachau did not find any harmful effects of such a combination in treatment.

GOODMAN, New York.

ROENTGENOTHERAPY OF ACTINOMYCOSIS. A. E. RUETE, Dermat. Ztschr. **32**:344 (April) 1921.

Ruete has found that doses as large as those recommended by Klemm in an earlier number of the *Zeitschrift* are unnecessary. He gives dosages of approximately one third less with good results. The measurements are given in a foreign scale, probably Kienbeck's, as follows: Klemm recommends two sessions at 20 cm. skin-focus distance with 3 mm. of aluminum for 27 X repeated five times to a total of 100 X. Ruete's patients received a total of 35 X. This was repeated in deep seated cases. The argument is advanced that roentgenotherapy should be accomplished with the smallest dosage which is effective.

GOODMAN, New York.

TREATMENT OF FURUNCULOSIS IN INFANTS. C. G. GRULEE, and C. B. ROSE, J. A. M. A. **77**:37 (July 2) 1921.

Impressed with the inadequacy of the commonly used methods for treating this condition, the authors have tried roentgen-ray treatment. After some experience they found that a soft unfiltered ray (3 milliamperes, 6 inch spark gap, 9 inch focal distance, for one minute) was best. Their general impression as to the results of roentgen-ray treatment has been, on the whole, favorable; but their cases have been too few to reach definite conclusions. They feel, however, that the proper use of the roentgen ray may add materially to the efficacy of treatment for furunculosis in babies.

MICHAEL, Houston, Texas.

ACCIDENT AS THE CAUSE OF ACRODERMATITIS ATROPHICANS AND ARTHRITIS DEFORMANS. E. MEIROWSKY, Dermat. Ztschr. **32**:346 (April) 1921.

A young soldier who was admitted to the Army free of any defects developed typical acrodermatitis chronica atrophicans and arthritis deformans after an accident to his foot. In what fashion the accident caused the acrodermatitis is difficult to decide. The answer of trophoneurosis is the one usually given.

GOODMAN, New York.

THE TESTES AND CERTAIN VASOMOTOR REACTIONS OF THE PENIS. A. C. CRAWFORD and J. M. GEORGE, J. Urol. **5**:89 (Feb.) 1921.

The authors' work consisted in experimentation on dogs, using various drugs as well as testicular and other tissue extracts, to determine the constrictor or dilator action on the penis. They conclude that the testes have a specific substance that produces such dilatation.

JAMIESON, Detroit.

A METHOD OF DEMONSTRATING CATALYTIC ENZYMES IN INFECTED HAIRS. T. H. C. BENIANS, Proc. Roy. Soc. **14**:69 (June) 1921.

The suspected hair is placed in about twenty volumes of hydrogen peroxid on a slide and under a cover slip. When tinca infection is present, a vigorous effervescence persists for from fifteen to thirty minutes. The root of the hair must not be included because it normally will effervesce. (The same

reaction may be expected in other infections in which "catalytic" enzymes are present, and therefore the method can hardly be of value in differential diagnosis.)

GUY, Pittsburgh.

IDIOPATHIC PURPURA WITH UNUSUAL FEATURES. A. S. ROSENFELD, *Arch. Int. Med.* **27**:465 (April) 1921.

Two cases are described by the writer which showed a familial tendency and repeated joint hemorrhages which had an association with the symptoms of Henoch's purpura. One case also had a spontaneous fracture.

JAMIESON, Detroit.

DERMATITIS HERPETIFORMIS. E. G. LITTLE, *Proc. Roy. Soc.* **14**:69 (June) 1921.

A woman who had been bitten on the finger by a rat six years previously and had had a resultant rat-bite fever that persisted for a year developed an extensive eruption of vesicles with pigmentation and intense itching a year later. A pronounced indicanuria and a marked eosinophilia were noted. The patient was unusually susceptible to arsenic so that proper medication was a problem.

GUY, Pittsburgh.

A CASE OF ACRODYNIA. P. W. EMERSON, *J. A. M. A.* **77**:285 (July 23) 1921.

A boy, aged 4½, developed general weakness, loss of knee reflexes and redness and peeling of the finger tips and toes; the redness, extending over half the first joint, diminished gradually from the tip backward. On one toe, there was a vesicle-like lesion. The constitutional disturbances consisted of marked apathy and muscular weakness, with moderate fever.

Complete recovery ensued in about four months.

MICHAEL, Houston, Texas.

RADIUM BURN. E. G. LITTLE, *Proc. Roy. Soc.* **14**:68 (June) 1921.

A man, aged 50, who had had radium applied over his spine for twenty-four hours, ten years ago, developed an extensive scar which three months ago broke down to form a deep ulcer. The presenter considered the condition malignant.

GUY, Pittsburgh.

TREATMENT OF WEEPING ECZEMAS WITH LENIGALLOL. L. ISAACSON, *Deutsch. med. Wchnschr.* **47**:653 (June) 1921.

Lenigallol, a compound of acetic acid and pyrogallol, is used in the following ointment:

	gm. or c.c.
Lenigallol	1.5
Zinc oxid
Olive oil	ad 25.0

AHLWEDE, Hamburg.

Society Transactions

AMERICAN DERMATOLOGICAL ASSOCIATION

Clinical Session, June 2-4, 1921

JAY FRANK SCHAMBERG, M.D., *Presiding*

ULCERATIONS OF THE LOWER LIP. Presented by DR. WHITE.

A man, aged 52 years, had been in the United States Navy for twenty-five years, had traveled all over the world and had passed the Island of Guam, but had never stopped there. He had had ample opportunity to contract some tropical disease. The disorder began five years ago in Cuba after he had wounded the lip by rapidly removing a clay pipe. He had received treatment of all kinds, including arsphenamin, to no effect. The case had been investigated by many different men, and the navy department had sent tissue to Washington, D. C., for examination, but nothing had been found outside of "chronic inflammatory" tissue.

The condition was thoroughly enigmatic objectively. The lower lip had entirely disappeared, and the remaining tissue disclosed nothing which indicated any of our well-recognized diseases. Wassermann tests had always proved negative.

DISCUSSION

No diagnosis was offered.

MULTIPLE XANTHOMA. Presented by DR. TOWLE.

A boy, aged 3 years, had had an affection since earliest infancy. As seen, it involved the scalp, neck, trunk and extremities. At first few, the tumors had gradually increased in number and had involved more and more territory. The primary lesion was small, perhaps pea-sized and by steady gradual growth, it had attained a maximum size of about 1½ by 1 inch. Some of the lesions were round, though many were oval in shape. Their tops were rounded so that in some it was fully one-half inch from the highest point to the level of the surrounding skin. In shape the lesion reminded one strongly of a beetle. The color was a curious yellow. To the touch, the tumors were firm although not hard. Histologically the tumors were xanthoma.

As to treatment, under heliotherapy a number of the tumors had disappeared. Others had shrunk in varying degree.

DISCUSSION

DR. PUSEY agreed with the diagnosis. He thought that Dr. Towle and Dr. White should receive an expression of appreciation for the opportunity of seeing their patients. Dr. Towle's case was unique so far as manifestations of xanthoma were concerned in his experience. He asked whether there was any disturbance in the general health.

DR. TOWLE said that the diagnosis had been confirmed by histologic sections. Some of the lesions had disappeared under heliotherapy. There was no disturbance in general health, but the cholesterol content of the blood was very high, three times that of the normal child of that age.

MULTIPLE PIGMENTED NEVI. Presented by DR. OLIVER.

A boy, aged 1 year, presented numerous unusually black nevi scattered over the body. The largest single lesion covered the entire back. The lesions had been present since birth and were of inky blackness. The skin appeared normal except for the pigmentation.

DISCUSSION

DR. RAVOGLI said he had seen three or four cases of melanosaarcoma which had started from nevi, black pigmented spots spread all over, and the patients had died within a short time. He thought this was a case of melanosaarcoma.

CONGENITAL ALOPECIA. Presented by DR. WHITE.

A boy, aged 2 years, had complete alopecia. The nails and teeth were normal. There were no similar cases in the family history.

DISCUSSION

DR. McEWEN called attention to the reports of congenital alopecia by Dr. Hyde, in which two of the patients had webbed toes.

EPIDERMOLYSIS BULLOSA (AVEC KYSTES EPIDERMQUES).

Presented by DR. WHITE.

The patient was a child, aged 2 years. The disease began at the age of 5 days and had persisted ever since.* In addition to the bullae which had often been hemorrhagic, the child presented the "kystes epidermiques" of Hallopeau. The knees, elbows and knuckles were a mass of contiguous, cigaret-paper like, pea-sized scars. Many of the nails were gone, and at presentation there was a hemorrhagic bulla on the palm as the result of a fall on the previous day.

Thyroid therapy had been started on May 25, and the mother stated that since that time there had been fewer bullae and that the child's condition was better.

DISCUSSION

DR. SUTTON was interested in this condition because of the curious histologic picture (absence of elastic fibers) presented by many, if not all, of the patients with congenital cases. He believed, however, that Dr. Fred Wise had failed to find this anomaly in the cases that had developed in adult life.

With regard to the spelling of the term, fourteen years ago, he had discussed the matter with Dr. Achilles Rose of New York, at that time probably our greatest living authority on medical nomenclature, and Dr. Rose had informed him that it should be "epidermidolysis bullosa" and not "epidermolysis bullosa."

CONGENITAL ALOPECIA. Presented by DR. TOWLE.

A boy, aged 2 years, presented a complete absence of hair on the scalp, eyebrows and elsewhere on the body. There was also a certain dystrophy of the nails and a tendency toward recurrent paronychia. From time to time lanugo hairs had appeared, whose life, however, was short. At no time had there been any normal hair.

DISCUSSION

DR. WENDE recalled that at a meeting in Boston in 1902 he read a paper describing a similar case—almost a counterpart—under the title of "Epi-

dermolysis Bullosa Hereditaria," with congenital alopecia, dystrophy of the nails and inflamed areas about the mouth. The condition about the mouth he thought was due to the irritation of the skin as the child drooled; the drooling being due to the irritation and bleb formation within the mouth as the result of food trauma. The rarity of this disease is great; apart from Dr. Towle's case he could recall only one other; reported in the ARCHIVES. These three cases all have the same external clinical features and undoubtedly should be classed as "epidermolysis bullosa hereditaria."

RINGWORM. Presented by DR. WHITE.

A boy, aged 7 years, who presented a type of ringworm not often seen in Boston, came in with a few pustules, or pustular remains, and all around the bald, slightly infiltrated, dull red center there was a rim of crusting. On cultivation violaceous growths were produced.

EPIDERMOPHYTOSIS. Presented by DR. WHITE.

A man, aged 50 years, had had the disorder constantly on the feet for five years, whereas on the hands it had developed more recently and had come and gone. At the time of presentation he had a severe outbreak presenting a contiguous mass of pinhead-sized or smaller vesicles on the lateral aspects of the fingers and on the adjacent palms and backs of the hands and fingers. The itching was intense. The feet were less intensely affected. Here there was mild vesiculation about the toe and exfoliation extending backward onto the ball of the feet.

DISCUSSION

DR. WILLIAMS thought such a case was very interesting, particularly the presence of the disease on the sole under the instep. It was hard to conceive of the organism spreading so rapidly as to involve both hands and feet in a few hours, but the rapid spread of the eruption does occur. He thought that a better explanation of the spread of the eruption was the distribution by the circulation of toxin absorbed from the primary focus of the disease. He thought chances of finding the organism of the lesions of the feet were much greater than in those of the hands, and he believed the condition on the latter was toxic rather than mycotic.

DR. RAVOGLI thought it was a case of occupational dermatitis. The man worked seven days a week in a shoe factory, and probably in handling the leather would irritate the skin and produce a dermatitis.

DR. WENDE thought every one should be familiar with this type of eruption as it was characteristic of the epidermophyton eruptions.

MYXEDEMA. Presented by DR. TOWLE.

A woman, aged about 35 years, for several years had been under treatment at the Massachusetts General Hospital for myxedema and had been under constant thyroid therapy. For some months there had been recurrent swellings on both cheeks, which had come and gone with irregularity. The present manifestations had been present for about two months. On both cheeks, over the flush areas, were patches of considerable size, which had the clinical characteristics of acute lupus erythematosus.

DISCUSSION

DR. HIGHMAN thought the lesions looked like lupus erythematosus, and asked whether there had been any improvement.

DR. GOLDENBERG thought it was a superficial type of lupus erythematosus.

DR. WILLIAMS thought the spots just below the ear were almost a counterpart of a case presented recently by Dr. Whitehouse. He agreed with Dr. Goldenberg that it was lupus erythematosus, and doubted whether there was any connection with the thyroid gland. He was particularly interested in the presence of the small papule in the right cheek. This resembled rosacea, but was not the same. The case of Dr. Whitehouse presented papules sometimes covered with a crust, and Dr. Williams wished to know whether the other gentlemen had seen an eruption of soft papules of this type in connection with lupus erythematosus.

DR. TOWLE said the patient was shown because of a deficient thyroid gland. She was taking thyroid extract all the time, and the eruption developed during this medication. He wished to contrast this patient with the child whose eruption had cleared up following thyroid therapy, in an effort to determine if possible whether there was any connection between hypothyroidism and the eruption.

LYMPHANGIOMA OF THE TONGUE. Presented by DR. OLIVER.

The patient was a man aged 28 years, whose lesion, which had persisted for five or six years, involved practically the whole tongue. The tongue was twice its normal size.

The patient was to be placed on radiotherapy.

DISCUSSION

DR. COLE said they had recently had two cases like this at Lakeside Hospital. One of the men from the Mayo Clinic had said that better results were obtained with roentgen rays than with radium. Roentgenotherapy had been used in his cases with good results. One patient was a girl, aged 5 years, with a lymphangioma which involved the right side of the tongue so extensively that she could not get the tongue back in the mouth. She was given two treatments with roentgen rays, two weeks apart, a small dose being used and no especial cross-firing. There was a marked change after the first treatment, and the child could now get her tongue back in her mouth. He suggested the use of roentgenotherapy rather than radium in this case.

DR. PUSEY said he thought there was no difference in the results with radium and roentgen rays, except as the amount of soft rays would vary. He thought it was important to get essential facts in mind. In his judgment, so far as the actinic effects were concerned, there was no difference. He would prefer radium in this case because it was more convenient to use, but the essential thing was that there was no difference in the actinic effect in the two agents. In his opinion the more unnecessary confusion that was avoided, the less trouble there would be in the future with the two agents.

TUBERCULOSIS. MULTIPLE FORMS IN A SINGLE PATIENT.

Presented by DR. TOWLE.

A colored woman, aged 23 years, originally had a scrofulous gland on the right side, and traces of the scrofulous tuberculosis were still visible. Later there had developed a tuberculosis cutis of the right lower lid involving the

tear duct and gland, which still showed activity. On the right cheek was a large patch of typical lupus vulgaris. On the left forearm was a hard brownish-red nodule the size of a small pea, which represented the persisting local reaction to tuberculin injections.

EPITHELIOMA OF THE CHEEK. Presented by DR. C. GUY LANE.

A man, aged 67 years, showed a healed epithelioma of the cheek. The lesion had been present on his left cheek for eight years when he was first seen at the clinic eight months previously. At that time the tumor was about 1 by 1½ inches in size, crusted, hard and elevated one-half inch above the surface. He had received seven hours of radium therapy with a half strength applicator unscreened, and two hours of treatment with the same applicator using a 0.3 mm. brass screen. The lesion now showed a smooth, purplish healed scar without any crust and without any sign of induration.

MYCOSIS FUNGOIDES. Presented by DR. TOWLE.

A woman, aged 50 years, had had the disorder for three years. When she presented herself three years previously, the body was covered with almond-sized, hard, resistant tumors. Several of the growths had been excised, and all gave the picture of mycosis fungoides. The skin surrounding the lesions was dry and flaky, and from the skin arose the little masses, perhaps a dozen in one area, then an open space and then another group. Stains of old lesions were still visible.

Roentgenotherapy had been used exclusively, and under its influence the disease had largely cleared up. No new lesions had developed in several months. The treatments, of which she had received ten or twelve, were each of $\frac{1}{8}$ or $\frac{1}{10}$ unit, the highest dose having been $\frac{1}{4}$ unit. She had had some reaction following treatment, and the smaller doses worked better than the larger ones. The reaction consisted of an erythema which resembled sunburn, then actual vesiculation, the changes occurring within twenty-four hours after treatment.

PITYRIASIS RUBRA PILARIS. Presented by DR. OLIVER.

A woman, aged 53 years, had had the disorder for nine months. It appeared immediately after a severe shock. It began on the forehead and had gradually spread until it involved practically the entire body; it was still spreading.

The use of the quartz light had relieved the itching and thinned out the skin to some extent.

ACUTE LUPUS ERYTHEMATOSUS. Presented by DR. TOWLE.

A woman presented lesions of lupus erythematosus of the acute, diffuse type. The disorder was of four months' duration.

DISCUSSION

DR. SUTTON said he did not know the cause of lupus erythematosus. This patient undoubtedly was suffering with several bad teeth, and he believed the teeth should be roentgenographed. It was always well to clear up all foci of infection. The fact that lupus erythematosus is practically unknown in the sanatoriums around Denver would indicate that it was not necessarily related to tuber-

culosis. Dr. Hartzell has reported a case that was cured following the removal of infected teeth. Dr. Sutton made it a point to remove infected tonsils and infected teeth; he had obtained some good results; he was sure a much larger percentage of recoveries had taken place since they had followed this plan.

DR. MCEWEN stated that in the *British Journal of Dermatology* a number of reports by Barber had appeared in the last year in which *Streptococcus longus* had been found in culture of the stools and in the tonsils; vaccines prepared from cultures had caused reactions locally in the areas involved.

DR. HIGHMAN said he had seen several cases of lupus erythematosus in patients with full sets of false teeth.

DR. CHIPMAN, in answer to Dr. Highman's remark, said he had seen people who wore two complete plates of teeth and yet focal infection was seen underneath, because the mere extraction of teeth does not necessarily eradicate focal infection. He thought this of great importance in lupus erythematosus. The most dramatic dermatologic result he had ever seen was the disappearance of lupus following the surgical removal of six or seven teeth. He believed the profession was guilty of serious laxity when the foci were attacked by simple extraction. The teeth should be surgically removed in the proper manner.

DR. JOHN E. LANE took exception to Dr. Sutton's remarks in which he intimated that because lupus erythematosus is not frequent in tuberculosis sanatoriums it is not a tuberculous process. He considered that argument of no value because skin tuberculosis of any description is quite rare in tuberculosis sanatoriums. He had looked for it in several, and had made many inquiries as to its frequency of physicians in charge of such sanatorium. The question of the relationship of lupus erythematosus to tuberculosis would have to be settled in some other way.

EPITHELIOMA OF THE WRIST. KERATOSIS OF THE FACE.

Presented by DR. TOWLE.

On the face of a woman aged 64 years were some ordinary keratoses. On the wrist was a large ulcerative lesion which offered considerable difficulty in diagnosis, which was only cleared up by the microscope. The lesion consisted of concentric whorls of hard epithelial ridges enclosing a central, crusted ulcer. The whole was considerably raised above the general surface and was nearly 3 inches in diameter.

At first the diagnosis of a manifestation of syphilis was considered, but the microscope revealed that it was a basal-cell epithelioma.

A CASE FOR DIAGNOSIS. Presented by DR. TOWLE.

A woman, aged 63 years, was seen for the first time on the day of presentation. She had been in the hospital before for treatment of a throat condition, which proved to be an epithelioma. The interesting part was that the lesion looked like lupus vulgaris, and, although it had been present only three years, it had degenerated into an epithelioma.

There was complete destruction of the uvula, which it was thought was caused by tuberculosis. The alae of the nose showed extensive ulcerative tuberculosis. On the right cheek was also a coin-sized ulcerative ulcer. No active tuberculosis was found in the lungs, although with the roentgen ray there were signs indicative of an old, healed process.

DISCUSSION

DR. PUSEY thought it was syphilis.

DR. POLLITZER thought it was tuberculosis.

DR. McEWEN asked whether the condition of the tongue had been proved to be carcinoma.

DR. CORLETT thought that in hazarding an opinion as to the diagnosis, the first would be syphilis and the next tuberculosis.

DR. TOWLE said the condition for which the woman had first entered the hospital was an epithelioma. He thought the present condition was due to tuberculosis, as there was neither history nor evidence of syphilitic infection.

LESIONS ON THE EAR, NECK AND BACK OF THE SHOULDER.

Presented by DR. SMITH.

A woman, aged 47 years, when first seen had lesions back of the ear like the large, shiny papular lesions of syphilis. There were large, circinate lesions on the inside of the thighs and over the left breast. There was no history of syphilitic infection, but on the possibility of its being syphilis she was given four or five injections of arsphenamin, without any particular effect. The appearance of the lesions and the scarring were consistent with a late syphilid, but Dr. Smith thought they were probably tuberculous in character.

DISCUSSION

DR. CORLETT said that clinically the lesion over the scapula was distinctly tuberculous in appearance and that some of the later lesions elsewhere were typical of lupus. Some of the shiny patches which had appeared more recently had a striking resemblance to lichen planus. Dr. Smith had suggested that those lesions had undergone involution and that the lesions which appeared to be quite flat would subsequently assume the appearance of the typical lesions of lupus, which he thought explained the apparent incongruity, and, therefore, he would regard the case as one of tuberculosis cutis.

DR. PUSEY agreed with the diagnosis. He thought it was a case of lupus erythematoïdes.

DR. ORMSBY said the lesions on the thigh were typical tubercular nodules like the others. Erythematoïd lupus vulgaris presents a very different picture, and he did not consider this case an example of this type.

DR. PUSEY said lupus erythematoïdes was not a combination of these two but a lupus vulgaris with the appearance of lupus erythematosus—erythematosus-like lesions, but not a combination or mixed type.

DR. HIGHMAN thought the lesions resolved themselves easily into lupus nodules.

DR. POLLITZER said the first case of lupus vulgaris erythematoïdes was published by Leloir in 1890 and represented a disease which at first glance was lupus erythematoïde, more or less extensive plaques with scaling, which, on close inspection, presents something of the appearance of lupus vulgaris. A diagnosis was possible from the histologic structure and experimental inoculations rather than the clinical picture.

DR. GOLDENBERG thought the colored girl with the three phases of tuberculosis had a typical case of Leloir's lupus vulgaris erythematoïdes.

HODGKIN'S DISEASE. Presented by DR. WHITE.

A man, aged 30 years, presented multiple pea-sized and larger nodules distributed over the body and extremities. There were literally hundreds of these round and almond shaped tumors which were firm but not hard and produced no change in the color or the texture of the overlying skin.

The patient had been sent up from the medical ward for diagnosis of his cutaneous symptoms. There was a history of "stomach trouble" of eight years' duration and of a strongly positive Wassermann reaction.

Blood examination made in the hospital revealed 2,784,000 red cells and 2,400 white cells; the color index was 0.98; hemoglobin content was 53 per cent. (Sahli). The differential count was: 94 per cent. large lymphocytes, 4 per cent. small lymphocytes and 2 per cent. polymorphonuclears.

DISCUSSION

DR. SCHAMBERG believed it to be a case of leukemia of the skin.

SARCOMA. Presented by DR. WHITE.

A man, aged 60 years, who presented lesions on the left leg, had a history of a street-car accident in November, 1920. In February, 1921, two nodules began to appear on the left leg and had persisted since that time. These were quite alike and consisted of decidedly hard, protuberant masses the size of mandarin oranges and the color of raw beef.

DISCUSSION

DR. HAASE said regardless of the fact that some of the lesions had disappeared he believed they were sarcomas.

PSORIASIS. Presented by DR. OLIVER.

A man, aged 33 years, presented lesions of psoriasis that were limited to the abdomen and back, covering large areas in these situations.

PRIMARY LESION OF THE TONGUE. Presented by DR. SMITH.

A man, aged 54 years, who worked in a large industrial plant where a common drinking cup was used, had been admitted to the surgical ward for a supposed epithelioma of the tongue. There he was seen in consultation and a diagnosis of a primary lesion of the tongue was made. He received two injections of arsphenamin within three or four days; then he was put on weekly treatments, and the condition cleared up and remained well for some time. He then returned with a strongly positive Wassermann reaction and received another course of treatment. Following that he developed a generalized exfoliative dermatitis which, in the course of six weeks, subsided, and his general condition became good in two months. Following that there gradually developed a parakeratotic condition, definitely margined and quite pruritic, and the clinical picture was that of parakeratosis verging into mycosis fungoides, but sections from the infiltrated areas showed only the marked parakeratosis. Dr. Towle said that the tumors were identical with those of the woman he had exhibited.

DISCUSSION

DR. WILE thought it was lichen planus. He thought the lesions on the buccal mucosa and on the glans penis were typical of lichen planus. The hyperpigmentation might have been due to the arsenic.

Dr. GOLDENBERG agreed with Dr. Wile's diagnosis.

Dr. FORDYCE thought it was well for the members of the Association to read up on the arsenic epidemic which occurred in England twenty years ago from poisoning of the beer supply. The description of the skin lesions during that epidemic would correspond to the lesions in this case. There was thickening of the skin, and bullous and pustular lesions without the chronic effect of arsenic on the skin.

Dr. SUTTON said that in the beer cases there were no lesions on the mucosa of the mouth.

Dr. ORMSBY called attention to the fact that the lesions in the mouth extended along the margin at the junction of the teeth. These lesions were not individual, but were plaques identical with those commonly seen in leukoplakia. He had seen the cases of arsenical dermatitis in London, and a number of the lesions on this patient's skin simulated those very closely. He could not see any lesions that could be definitely said to be those of lichen planus. A biopsy had been made which did not show the structure of lichen planus, and the latter is a disease that can be diagnosed microscopically.

Dr. HIGHMAN thought it was curious how people looking at the same thing formed such different ideas of what they saw. He did not pay much attention to the skin of this patient after looking in the mouth and seeing the typical lesions of lichen planus. He thought the lesions on the skin were involuted lesions of lichen planus. The color of the lesions on the lower part of the trunk seemed quite characteristic of faded lichen planus, and the typical lesion on the glans penis seemed to him to satisfy all the phases of the question that needed to be satisfied.

HYPOTHYROIDISM. Presented by Dr. TOWLE.

The patient was a child, aged 4 years, whose case is reported in detail in a paper entitled "Hypothyroidism with Unusual Skin Manifestations," to be published in the ARCHIVES.

LUPUS VULGARIS WITH ELEPHANTIASIS OF THE FACE. Presented by Dr. TOWLE.

A boy, aged 17 years, who lived in a rural New England village, four years ago suffered a mild frostbite of both cheeks. Three years ago, during the cold weather, both cheeks swelled and an eruption developed. With the onset of warm weather the swelling disappeared. The symptoms recurred with cold weather and disappeared with warm weather. Last winter the swelling recurred as before, but this spring it failed to disappear.

On entrance to the hospital the boy presented an upper lip which was so swollen as to impinge on the nostrils. From the ala on either side an outwardly curved band of ulceration ran downward to the corners of the mouth. Within, the surface was bluish-red and studded with pinhead to pea-sized greenish-yellow crusts. At either corner of the mouth was a lesion, 1 inch in diameter, which clinically suggested epitheliomas. On palpation the swollen lip gave a sense of deep fluid infiltration. Nowhere were there visible any typical lupus nodules, but under the microscope typical tubercles were present.

Hot and cold boric acid wet packs had caused the swelling of the lip to lessen greatly, and after the use of the quartz lamp, pyrogallic preparations and various other caustics the tuberculous lesions had improved.

DISCUSSION

DR. SUTTON thought the condition looked like lupus vulgaris.

GENERALIZED DERMATOSIS. Presented by DR. BURNS.

The patient was a man, whose disorder began fifteen years ago, appearing first on the face. Gradually, with varying remissions, it spread to the trunk, the upper limbs, and to a small extent to the lower limbs. The process was characterized by infiltrated, papular lesions, followed almost invariably by a certain amount of atrophy. When the patient was first seen in consultation, Dr. Burns was inclined to call the condition a case of dermatitis chronica atrophica, although it was not typical of this disorder. He had had no opportunity to examine the patient carefully since that time, as he had just returned to the hospital.

DISCUSSION

DR. LANE said it had been suggested that this might be a case of poikiloderma atrophicans vasculare. He thought that possible and that a further study would be necessary for decision of the question, because the cases so far reported were too few to have definitely fixed the limits of the variation of appearances in that disease. This case, however, showed some marked differences from his case and those previously described. The most striking difference was that in this case the most marked changes were at the edges rather than at the center of the lesions. In other cases there was marked lividity at the center of the older lesions. This was absent here, and there was also little atrophy. The pigmentation of this case was less distinct than in previously reported cases. He hoped that Drs. Wise and Ormsby would give their impression of the case.

DR. RAVOGLI said the case impressed him with the possibility of Majocchi's disease on account of the discoloration and the small nodules disposed in circles in the hand. He thought it was probably an aggravated case, which had after a long time caused atrophy of the skin.

DR. ORMSBY considered the case entirely different from anything he had ever seen. While in some respects it resembled the case they had had under observation, in other respects it was very different. In their case the lesions resembled a healed radio-dermatitis, but in this case no lesions of this type were present. He could not be sure that there was telangiectasia and, taken as a whole, the case was very different.

DR. WISE thought the interpretation of the case was almost impossible without further study. In regard to Dr. Ravogli's statement that it might be Majocchi's disease, that could be eliminated. Those cases had not widespread atrophy, and in this patient it would be courageous to say that it was more likely that disease than any other clinical conception of anything in the literature. He believed further study would prove it to be that disease. Five years from now the skin may take on the typical appearance of Dr. Lane's case, and resemble an old cured radiodermatitis, which poikiloderma resembles.

DR. FOERSTER said that in the *Ikonographia* a case is described by Jamieson without diagnosis in which the clinical picture bears resemblance to this condition in several respects.

DR. PUSEY asked whether there was anything in Dr. Lane's case of poikiloderma analogous to the infiltrated appearance which precedes the atrophy in these cases.

DR. LANE said there was never any elevation of the skin in his case. The new lesions, where the process was spreading, were first pigmented around the hair follicles; then the inflammatory process appeared and later the atrophy.

DR. PUSEY thought this patient would not have telangiectasia later for he did not have that kind of skin. The infiltrative process at the border was probably the primary process. He could see no evidence of secondary telangiectasia.

DR. McEWEN said the patient told him the process had been going on for fifteen years.

DR. LANE said that in his case every one had remarked on the resemblance to angioma serpiginosum. There was no such likeness in this case.

DR. BURNS said the patient was seen first in the surgical ward in consultation. Only a short examination had been made at that time and he asked to have the man transferred to the dermatologic ward when discharged. The tissue instead of being sent to him was sent to the general laboratory and was lost. They hoped to be able to elucidate some of the points brought up by the discussion. In presenting the case he felt embarrassed because he had had no opportunity to study the patient and had no adequate history, so presented the case for diagnosis. The disorder had been present for fifteen years.

DR. HAASE said that without ever having seen a similar case, he would hazard a diagnosis of a diffuse tuberculosis of the skin of some form, advancing, leaving scar tissue behind.

DR. WALLHAUSER agreed with Dr. Haase. The peculiar lupoid nodular border was strongly suggestive of a tuberculous process.

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Archives of Dermatology and Syphilology

VOLUME 4

NOVEMBER, 1921

NUMBER 5

POIKILODERMA ATROPHICANS VASCULARE *

WITH REPORT OF A CASE BY OLIVER S. ORMSBY, M.D., CHICAGO

JOHN E. LANE, M.D.

NEW HAVEN, CONN.

At a meeting of the New York Dermatological Society, May 25, 1920, attended by all but one of the members, I presented a patient for the diagnosis of a curious and complex dermatosis, with which I was unfamiliar. The eruption consisted of telangiectases, petechiae, pigmentation, atrophy and ulceration. No similar case has been seen by any of the dermatologists present, but Dr. Fred Wise suggested the diagnosis of poikiloderma atrophicans vasculare and compared the appearance of the lesions of the patient with the cuts of the first case reported under that name by Jacobi. This diagnosis was confirmed by the study of previously reported cases of that dermatosis, of which twelve have been found, nine in the German, two in the French, and one in the Russian literature.

The reported cases vary to a considerable extent in many details, but the predominant characteristics common to all are: redness, caused by dilatation of the minute superficial vessels of the skin, reticulated pigmentation and more or less diffuse atrophy.

The extreme rarity of the disease, and the fact that there is nothing on the subject in English, are perhaps sufficient reasons for reviewing the literature and abstracting the previously reported cases. It was impossible to make a complete study of my case because of the patient's refusal to submit to a biopsy, but through the courtesy of Doctor Ormsby I am permitted to include the case report of one of his patients from whom he was able to obtain material for a histologic examination.

REPORT OF CASES

CASE 1 (Reported by Petges and Cléjat¹ in 1906).—This case was described under the name of atrophic sclerosis of the skin, and was associated with generalized myositis and tuberculosis of the lungs. The case came to necropsy

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Petges et Cléjat: Sclérose atrophique de la peau et myosite généralisée, Ann. de dermat. et syph. 7:550, 1906.

and was studied in detail, but space prevents the description of any lesions except those of the skin.

History.—The patient was a working woman, aged 30. The eruption had started two years before, with swelling of the left side of the face, the neck and the left arm. When the patient was first seen a diagnosis of angioneurotic edema was made, which was soon after changed to that of scleroderma.

Physical Examination.—There was a slightly sclerodermic appearance of the face, with a brownish color and slight scaling. The eyelids were reddish and swollen. On various parts of the trunk, the skin was a little thickened and tense. On the upper part there was a variegated appearance due to small brownish macules and a reddish marbling made up of a network of capillaries. The abdomen was less red, and the brown color was due to isolated spots of pigment, corresponding to the openings of the hair follicles. There was a similar appearance on the arms and hands, and in addition some atrophic spots similar to those which follow frost-bite, though there had been no previous ulceration. There was hypertrichosis of the arms. The legs and thighs were practically normal except for keratosis pilaris. Itching was intense in many of the affected parts.

Histology.—There was thinning of the epidermis and of the reticular layer of the derma, fibrous hyperplasia of the hypoderm and sclerosis of the sweat glands and of small islands of fat, which in some places were replaced by the fibrous tissue. The walls of the vessels of the hypoderm were thickened. The elastic tissue was abundant and massed in the upper layers of the derma and in the new formed fibrous tissue of the fatty layer. It was of normal structure and showed the reactions of elastin. The derma was richer in cells than normal, and in the tissue from the abdomen there were many pigmented cells. Some peculiar rounded hyalin bodies were also described, which have since been shown to be frequent in the atrophic dermatoses.

CASE 2 (Presented by Jacobi² at the German Dermatological Society in 1906, and more fully reported two years later³).—*History.*—The patient, a farmer, aged 30, had been treated four years before for pains in the joints and fatigue, which were still present. At that time he had also had edema with a peculiar bluish-red color of the face which was diagnosed as scleroderma. There were also present isolated scar-like changes in the skin resulting from scratching and superficial redness of the legs.

Physical Examination.—At the time of the report the scalp was scaly and showed atrophic spots the size of a lentil, surrounded by a hyperemic, pigmented network. The auricles were atrophic, tense and shiny, the face bluish-red to bronze and slightly puffy, the lower lids edematous, the neck a diffuse red, studded with telangiectases and partially covered with adherent scales. The back and chest showed widespread atrophic changes, atrophic spots of various sizes surrounded partly by dark pigmentation and partly by bright red to livid marbling, with numerous telangiectases and capillary hemorrhages. The hair follicles appeared as sharply limited reddish brown spots the size of the

2. Jacobi, E.: Fall für Diagnose (Poikilodermia Atrophicans Vascularis), Verhandlungen der deutschen dermatologischen Gesellschaft, IX Kongress, Bern, 12 bis 14 September, 1906. Berlin, 9:321, 1907.

3. Jacobi, E.: Poikilodermia Atrophicans Vascularis, Ikonographia Dermatologica, 1908, Fasc. 3, p. 95.

head of a pin. The appearance here was very much like that after an extensive roentgen-ray burn. On the trunk the skin was tense, thin and parchment-like, but freely movable and not sclerosed. The thighs were more deeply pigmented, but otherwise of similar appearance. The legs were of a livid color without distinct atrophy. On the arms and hands there were atrophic, hyperemic and cyanotic spots. There was hypertrichosis of both forearms. On the mucous membrane of each cheek there was a delicate whitish meshed spot, the size of a mark. Itching in the skin lesions was intense, especially at night.

Histology.—Infiltration of small cells around the dilated vessels and the glands was distinct. In the older lesions there was atrophy of all the layers of the skin, with rarefaction or disappearance of fatty tissue, atrophy and destruction of elastic tissue, alternating increase and absence of pigment.

CASES 3 and 4 (Reported together by Zinsser,⁴ in 1910).—*History.*—The first patient was a coachman, aged 21; the second, a brother of the first was 32. The two cases were so similar that the first only will be described.

The patient froze his fingers at the age of 4. This was followed by suppuration, shedding and regrowth of the nails, and the process was repeated until finally the nails were not replaced. A similar process had taken place in the toe nails. At the age of 17, the patient had had gouty pains in the knees and the right wrist, which later disappeared. His hands had been bluish, especially in the cold, since youth. The skin changes had been present for a few years.

Physical Examination.—At the time of the examination the nails of all the fingers were replaced by horny scars, the hands and forearms were cyanotic, bluish-red with white anemic spots of normal skin interspersed. The redness disappeared on pressure, showing in places a fine, regular, reticular pigmentation. The skin was not infiltrated, but showed slight reticular atrophy. The folds of the affected area were finer than those of normal skin, smooth, shiny and slightly depressed. There was hyperhidrosis of the palms and axillae. The appearance of the face and neck was similar to that of the hands. As far down as the collar, the skin was bright red, with pale, leukoderma-like spots, the size of a lentil; the redness was due to a fine capillary ectasia with pigmentation, which was seen by the use of the diascopé. Below the collar, there was no hyperemia but the pigmentation was more distinct and the skin was slightly scaly. The knees and elbows had a similar appearance. There was reticular pigmentation on the trunk, and it was especially deep in the axillae, groins and thighs. The nails of the toes were absent, the feet were cyanotic. There were leukoplakia-like changes on the mucous membranes of the cheeks and lower lip, a delicate mother of pearl thickening on the hard palate and a gray covering on the tongue.

Histology.—There was slight infiltration in the vicinity of the blood vessels of the cutis, scattered collections of extracellular and intracellular pigment, extending from near the vessels toward the epidermis, and diminution of elastic fibers.

4. Zinsser, F.: *Atrophia Cutis Reticularis cum Pigmentatione, Dystrophia Unguium et Leukoplakia Oris (Poikiloderma Atrophicans Vascularis, Jacobi)*. *Ikonographia Dermatologica*, 1910, Fasc. 5, p. 219.

CASE 5 (Presented by Müller⁵ at the Vienna Dermatological Society, in 1911; more fully reported the same year,⁶ and again shown by Finger⁷ at the second Congress of the German Dermatological Society in Vienna in 1913).—*History and Examination*.—The patient, a washerwoman, aged 25, with slight exophthalmos, and whose skin manifestations had been present for a long time, had red and edematous eyelids, the redness being due to telangiectases so small that an erythema was simulated. There was a similar appearance of butterfly shape on the nose and cheeks with reticulation and pigmentation. The skin was normal in the meshes of the reticulation. The skin was normal about the mouth. On the forehead were irregularly scattered macules forming circular or reticular figures, with normal skin in the interstices, and a few depigmented areas. On the upper part of the forehead was a large, evenly pigmented patch. On the front of the neck was a reticular, confluent erythematous spot with telangiectasia. Small, dimple-like atrophic spots extended in reticular form along the clavicle, where there was little normal skin, and delicate wrinkling and fine scaling were present. On the nucha the appearance was similar, but there was more pigmentation. There was a large whitish spot, with a livid undertone below the nucha. The outer surfaces of the hands and forearms were of a diffuse livid red with included spots of a livid white crossed by dilated vessels. There were depigmented spots on the elbows. There was a delicate network of fine whitish-gray lines with some telangiectasia on the mucous membrane of the cheeks.

Histology.—There was thickening of the keratohyalin layer, and hyperkeratosis, edema of the upper layers of the derma, distinct infiltration of lymphocytes, degeneration of elastic fibers and localized increase of pigment.

CASE 6 (Reported by Glück⁸ in 1913).—*History*.—The patient was a young man, age not stated, who was rachitic in childhood, had juvenile muscular atrophy, calcareous deposits over the tibia of the right leg, in the pectoralis major and larynx, and epilepsy, for which he continuously took bromids.

Physical Examination.—On the forehead was a patch of sharply limited redness with a bluish tone in which were some brown pigmented and some normal spots and numerous punctate dilated vessels. The eyelids were edematous, bluish-red, with some dilated vessels. Their pigmentation was normal. The nose and adjacent regions were brownish-red and showed single dilated vessels. The appearance over the chin and around the larynx was similar to that of the forehead. On the nucha there were in addition pigment changes showing

5. Müller, R.: Ein Fall von Poikilodermie (Atrophodermia Erythematoïdes), Wien. klin. Wchnschr. **24**:475, 1911. (Case presented at Wiener dermatologisch. Gesellsch., Feb. 3, 1911.)

6. Müller, R.: Atrophodermia Erythematoïdes Reticularis (Poikilodermia Atrophicans Vascularis, Jacobi), Arch. f. Dermat. u. Syph. **109**:501, 1911.

7. Finger: Case of Poikilodermia Atrophicans Vascularis, Arch. f. Dermat. u. Syph. **119**:171, 1914. (Case shown at the XI Kongress der Deutschen dermatologisch. Gesellsch., Wien, September, 20, 1913. This is the case shown and reported by R. Müller [Case 5]. It was presented by Finger, and discussed by R. Müller, Blaschko, Jadassohn, Weidenfeld, Zinsser and Herxheimer.)

8. Glück, A.: Dermatitis Atrophicans Reticularis (Poikilodermia Atrophicans Vascularis), mit mucinöser Degeneration der kollagenen Fasern, Arch. f. Dermat. u. Syph. **118**:113, 1913.

circular, white, vitiligo-like spots. There was redness with telangiectasia and wrinkling on both shoulders. Over the elbows, patellae and buttocks, the skin was red and slightly scaly. The skin of the hands and flexor surface of the forearms was slightly rough, more tense than normal, grayish-brown and slightly scaly. There were streaks of redness on the front and back of the forearms, and a bluish-red rosette-like appearance over the finger joints. Slight itching had been the only symptom. There were reticular opal white leukoplakia-like streaks on the mucous membrane of the lips, cheeks and gums, with telangiectasia.

Histology.—The appearances were those of atrophy and inflammation. The atrophic appearances were flattening of the papillae, breaking up and disappearance of elastic fibers, and changes in the collagen, consisting of both atrophy and myxomatous degeneration. The inflammatory changes were perivascular infiltration, dilatation of the vessels of the papillae and slight edema of the connective tissue.

CASE 7 (Presented by Schramek⁹ at the Vienna Dermatological Society, in 1912).—*History and Examination.*—The patient, a girl, aged 6, had shown the condition for two years. It had developed gradually without symptoms.

About the navel, extending toward the sides of the abdomen, was a delicate network of pigmented lines, in the meshes of which the skin was thinned, yellowish and slightly scaly. The thinning was apparently in the upper layers of the skin. There were similar patches in the left axilla, in front of the axillae, below the left nipple, around the angles of the scapulae, on the outer side of the right thigh, on the middle of the back of the left leg and on the left buttock. Some of the spots were sharply outlined, others indistinctly. The latter showed diffuse, uniform redness and swelling. There were many telangiectases in the spots on the back. The nails and mucous membranes were normal.

CASE 8 (Presented by Schramek¹⁰ at the Vienna Dermatological Society, in 1914).—The patient, a girl, aged 15 years, was presented for diagnosis. The clinical diagnosis lay between poikiloderma, lupus erythematosus, and scleroderma or morphea. (No description or discussion of this case was published).

CASE 9 (Reported by Terebinsky,¹¹ in 1916).—*History.*—The patient, a man, aged 34, a teacher, gave a history of having had neurasthenia, anemia, pulmonary tuberculosis and malaria. His skin condition had been present for eight years.

Physical Examination.—There were about thirty grayish-brown livid spots located on the front and back of the trunk, not affecting the groins and sacral region. Most of these spots varied in size from that of a dime to that of a silver dollar, but one on the lower part of the back was the size of the palm of the hand. The outline was somewhat irregular but sharply demarcated from the surrounding skin. Most of the spots showed whitish

9. Schramek: Case of Poikiloderma Atrophicans Vascularis, Arch. f. Dermat. u. Syph. **115**:394, 1913. (Case shown at Wiener dermatologisch. Gesellsch., Oct. 30, 1912.)

10. Schramek: Fall für Diagnose, Arch. f. Dermat. u. Syph. **119**:303, 1914-1915. (Case presented at Wiener dermatologisch Gesellsch., March 28, 1914.)

11. Terebinsky, V. I.: Poikiloderma Atrophicans Vascularis, Russk. Vrach. **15**:1057, 1916.

mottling. The older lesions were browner than the new ones, which were rather reddish-gray. Some of the spots had a distinctive livid color, partly due to telangiectasia. There was some atrophy, the skin showing slight wrinkling in the whiter parts of the lesion. When the skin was suddenly cooled, there was a very different appearance between the normal and affected skin. On the normal skin, goose flesh appeared, on the pigmented part of the lesion a few prominent follicles appeared, and on the whitish portion none at all. This demonstrated clinically the fact of the atrophy and destruction of the arrectores pilorum, which was borne out by microscopic examination.

Telangiectases were present in all lesions, especially at the border of the affected spots. There was a slight keratosis pilaris about the waist and in the groins. There was slight superficial scaling in a few of the older spots. There was no disturbance of sensation.

Histology.—Tissue from an early lesion showed the epidermis unchanged, the papillae normal, veins in the upper part of the derma, especially in the papillary layer, enlarged; capillaries enlarged and surrounded by infiltration of round and spindle cells with a few mast cells and an occasional plasma cell; increased number of nuclei in muscle fibers of arrectores pilorum, with disintegration of cytoplasm; increase of pigment in the lower epithelial structures; and no change in the connective and elastic tissue.

Tissue from an old lesion showed similar, but more marked changes. Circumvascular infiltration; endothelium of capillaries edematous, plasma cells increased, but not found in groups; connective tissue edematous, elastic tissue unchanged. The arrectores pilorum showed the most marked changes; they were thickened, the nuclei decreased; cytoplasm edematous and stained poorly; sweat glands small and atrophic. The hair follicles were atrophied and, in places, had disappeared.

CASE 10 (Presented by Civatte and Eliascheff¹² at the French Society of Dermatology and Syphilography, in 1919).—*History and Examination.*—The patient, a woman, aged 41, a cook, in whom the eruption, preceded by itching, had begun five years before on the face, neck and arms, had an eruption on the nucha, sides of the neck and over the mastoid regions but not on the ears. It stopped at the border of the hair and extended onto the pectoral regions, leaving the medi thoracic region unaffected. It extended onto the shoulders and forearms, fusing on the latter with an ordinary livedo.

On the neck were small macules, between which was sound skin. On the nucha was an irregular, complex network, with isolated macules at the edge of the patch. The macules and the network were brown and occasionally bluish and sprinkled with minute telangiectases. In the macules in which there was no telangiectasis, the appearance was that of an abundant eruption of ephelis or lentigo. In the mastoid region, the erythematous element was marked and resembled a brown marbling. Here there was little sound skin and the area was sprinkled with a multitude of small, projecting, white points, which were sebaceous glands showing through the thinned epidermis. The erythematous element was almost entirely absent on the temples, where the brown marbling was designed on a white, mother-of-pearl background of atrophic appearance, in which the follicles were unaffected and the orifices intact. On the shoulders,

12. Civatte, A., and Eliascheff: Un cas de poikilodermie, Bull. Soc. franç. de dermat. et syph., p. 185, 1919.

arms and forearms, the mixed design was very distinct, but was here due to superadded livedo, which had to be effaced to show the true eruption, which was hardly visible through it, and which was made up of yellowish, shiny, slightly depressed macules with no telangiectases. The macules had no evident connection with the livedo, but were grouped most abundantly in the meshes of the network. The eruption was pruriginous.

Histology.—There was superficial atrophy in various stages. When the atrophy was complete, the papillary layer was flattened, and the elastic layer did not extend to the basal layer but was separated from it by a thin, fibrous band. The corpus mucosum was normal and normally pigmented. In the areas in which the atrophy was not complete, there were more or less extensive islands in which a thick zone of amorphous or fibrous tissue, intersected by dilated vessels, lay between the corpus mucosum and the elastic network. There were lymphocytes around the vessels and, in places, small rounded lymphomas. There were also fusiform cells filled with pigment and clumps of irregular hyalin bodies. Below the fibrous zone the elastic network was wrinkled and massed at the upper edge of the derma, which showed no lesions. The epidermis was thinned, except in the superficial layers: the interpapillary bodies and stratum granulosum had disappeared. The layer in contact with the fibrous tissue was made up of flattened nonpigmented polyhedral cells, more or less dissociated by lymphocytes, and there were frequent small cavities containing lymphocytes, pigmentary granules and epithelial cells.

CASE 11 (Reported by Bruck,¹³ in 1919).—*History.*—The patient, a soldier, aged 41, had had a dry scaly skin from childhood. The eruption for which he presented himself had appeared at about the age of 7. A few years before he had had a mild attack of rheumatism.

Physical Examination.—Covering the whole body were two apparently unrelated conditions: 1. Over all of the trunk and the extremities with the exception of the joint flexures, the skin was rough and dry. The trunk was covered with whitish, branlike scales (Ichthyosis). 2. Over the whole body was a macular and reticular marbling which consisted of reddish surfaces and a network sprinkled with white spots. This marbling was diffuse over the whole trunk, and especially distinct over both shoulder blades and on the buttocks. It also extended over all the extremities. The face, hands and feet were free from the marbling, but on the forehead, the nose and the cheeks, there were numerous fine telangiectases without any inflammatory symptoms.

The variegated marbling consisted of reticulated, markedly dilated skin vessels, which partially disappeared under glass pressure showing numerous minute hemorrhages and extensive brownish-red pigmentation, especially at the borders of the white spots. The shiny white spots were atrophic and varied from the size of a lentil to that of a pfennig, and the hairs had disappeared on them. Nothing was found on the mucous membranes. The hair of the head and of the pubic region was thin, and it was almost entirely absent in the axillae. The nails showed no changes.

Histology.—The skin of the purely ichthyotic parts gave a typical picture of ichthyosis. Skin from the borders of the atrophic parts showed thinning of all the layers, flattening of the papillae, dilatation of the blood vessels, isolated

13 Bruck, C.: Ueber Poikiloderma Atrophicum Vasculare, Dermat. Wehnschr. 68:359, 1919.



Fig. 1.—Distribution of lesions on front of body in a case described by Dr. Lane.

and slight infiltration around the vessels, and marked increase of pigment which in other locations was almost entirely lacking. The elastic fibers were diminished and disassociated and in places had entirely disappeared. Connective tissue fibers were thin and lay horizontally but showed no degeneration. The hair follicles were atrophic and the subcutaneous tissue markedly thin. (This is a case of poikiloderma combined with ichthyosis).

CASE 12 (Reported by Bettmann,¹⁴ in 1921).—*History*.—The patient, a man aged 28, a turner, until recently had had no serious illnesses. He had passed the whole of the winter of 1915-16 in Russia, in the cold and damp. He had been in the hospital with furunculosis in the spring of 1916, and had had muscular rheumatism in 1918. He suffered with muscular weakness and fatigue.



Fig. 2.—Distribution of lesions on front of arm in case described by Dr. Lane.

Physical Examination.—There were fine pigmentations and telangiectases on the nose and cheeks. On the body were about a dozen patches distributed with approximate symmetry. The larger patches were on the right shoulder blade, left flank and right thigh. Jacobi's description was quoted as exactly applying to these lesions except that there were no capillary hemorrhages, no tenseness of the skin and no edema of the lids. There was a marked vascular network on the soft palate. The hands were not affected. There was no trace of scleroderma. The blood was normal, the Wassermann reaction negative, and there had been no previous application of roentgen rays.

14. Bettmann: Ueber die Poikilodermia Atrophicans Vascularis. Arch. f. Dermat. u. Syph. **129**:101, 1921.

Histology.—The epidermis was thin and flattened. The capillaries were dilated. In some areas there was marked cell infiltration of the papillary body. The infiltrate was limited to the papillary body and the superficial layer of the derma. The infiltrate consisted chiefly of lymphocytes and connective tissue cells. There were some branched mast cells. Leukocytes and plasma cells were not found. There were numerous connective tissue cells in which there was pigment which gave a bright grass-green color with polychrome methylene blue. The endothelium of the dilated blood vessels was not changed. The whole picture gave the impression of a wide-meshed network in which the cell elements were distributed. The elastic tissue was almost entirely absent from the infiltrated areas. In other places it formed a delicate ragged network which showed characteristic degeneration with the acid orcein stain. There was some degeneration of the collagen. There was no myxomatous degeneration, such as Glück found in his case.



Fig. 3.—Distribution of lesions on leg in case described by Dr. Lane.

CASE 13 (presented by Lane¹⁵ at the New York Dermatological Society, May, 1920).—*History.*—The patient, W. R. V-D., a chauffeur, aged 30, born in New Haven, was a well built man, 5 feet, 11 inches tall, weighing 155 pounds. He had had measles in childhood, and influenza in the winter of 1918-1919 and again in the winter of 1919-1920. He had had no other diseases except the dermatosis, which began about twelve years ago with a "red rash" on the back of the right thigh. This increased slowly until about a year ago, since which

15. Lane, J. E.: Case for Diagnosis, Arch. Derm. & Syph. 2:253 (Aug.) 1920. (Case presented at the New York Dermatological Society, May 25, 1920. Discussion by Drs. Whitehouse, Highman, Howard Fox, Wise and Winfield.)



Fig. 4 (Case 13).—Poikiloderma atrophicans vasculare. Distribution of lesions in case reported by Dr. Lane.

time the progress has been more rapid. There was no preceding edema. The development was quite symmetrical. There had been ulcerations on the upper inner surface of the right thigh and on the anterior and outer surface of the right leg about the middle. These ulcerations had healed slowly, and at one time the accidental separation of a scab from one of them was followed by a severe hemorrhage. The eruption was attended by some itching, which was worse if the lesions were allowed to dry. If kept somewhat greasy with an indifferent ointment, there was little discomfort. The patient had taken twenty drops of liquor potassii arsenitis daily for about six months, shortly after the beginning of the eruption. He had never had the roentgen ray applied; neither his brothers, sisters, parents nor grandparents had ever had any similar trouble.

Physical Examination.—This revealed a slight, soft systolic murmur at the second right interspace. The throat was red, and on the soft palate there were reticulated, dilated vessels; the left tonsil was large and adherent to the anterior pillar; there was no pigmentation. Many of the teeth had been extracted and several of the remaining ones were in bad condition. There was moderate obstruction of the nostrils. The axillary and pubic hair was sparse. Both feet were flat. The hemoglobin content and cytology of the blood were normal. The urine contained neither albumin nor sugar. The Wassermann reaction was negative.

Examination of the skin revealed nothing abnormal as regards the scalp, face, neck above the clavicles, hands and feet. Covering a large portion of the rest of the body was a nearly symmetrically distributed eruption presenting many different appearances in which the most striking features were telangiectasia, minute petechial hemorrhages, pigmentation, atrophy and ulceration.

On the anterior surface of the right arm the telangiectases and pigmentation were quite evenly distributed, covering the whole surface and extending on to the chest as far as the center of the clavicle and into the axilla. The telangiectasia was marked, and the whole surface was bright red, quite uniform for the most part, but in various places exhibiting small areas of normal skin showing as light points. Interspersed with the telangiectases were petechiae, in this and other locations in which the eruption was profuse. Towards the borders the eruption gradually faded, and the pigment was more easily seen, of a reddish-brown to brown. On the inner surface of the arm the eruption was less pronounced, and the telangiectasia and pigmentation more discrete and presented a somewhat reticular arrangement. In the bend of the elbow the reticular arrangement was quite striking, the small normal folds of the skin being of normal color and the skin between them being pigmented and the vessels dilated. The appearance of the inner and posterior surface of the forearm was about the same as that of the inner surface of the arm. The large veins on the inner and posterior surface of the arm were covered by normal skin and gave the appearance of white lines in the surrounding reddish area. The left arm and forearm had about the same appearance except that the arm was not so much affected as its fellow.

The medi thoracic regions, front and back, were not much affected. The rest of the chest was more or less covered with telangiectases and small spots of pigmentation, much less close together than on the arms, the waist being more affected than the other regions.



Fig. 5.—Distribution of lesions on front of body of patient in case reported by Dr. Ormsby.

The buttocks were covered, and the eruption here was evenly distributed and of uniform color, of about the same density as that on the forearms. The appearance of the posterior and the upper outer surface of the right thigh was similar to that of the arms, except that in many places the pigmentation and also the telangiectases were discrete and appeared as pinhead size points, of reddish brown, which appeared often to coincide with the openings of the hair follicles. There was no hair on the thighs, and the patient stated that there had never been any since he could remember. On the inner surface of the thigh there was a large oval patch, the borders of which gradually merged with the normal surrounding skin. As the center was approached the pigmentation and telangiectasia were more marked and atrophy was found, which appeared as light-colored, irregular spots, showing clearly in the surrounding deep red skin. At the center of this area was a scar of a healed ulceration about the size of a quarter of a dollar, with varicosities of the large superficial veins nearby. The skin in this and other atrophic spots was soft and pliable, with no sclerodermic hardening. The inner surface of the left thigh was of the same appearance as the right, except that the patch of deep pigmentation and atrophy extended over almost the entire surface as far as the knee, and showed no ulceration. The posterior surface was of a quite different appearance. It was entirely covered with a large patch, in the center of which the skin was thin and atrophied, shiny and markedly wrinkled. This part was of a uniform reddish-blue livid color. Just above the popliteal space the skin was of a deeper red, and the folds were exaggerated and contained a few small light colored atrophic areas and many large varicose veins. The appearance in the popliteal space was similar, and the varicose veins prominent. The popliteal space of the right leg was not so markedly affected, the appearance being similar to that of the buttocks. Varicose veins were distinct but not prominent.

The appearance of the left leg was for the most part similar to that of the arms and of the upper, outer surface of the right thigh; but there was an area of deep pigmentation, and atrophy with the scar, about the size of a quarter of a dollar, of a healed ulceration on the antero-external surface. There were distinct varicose veins on the inner side of the leg and some edema above the shoe line. There were the same edema, and the same varicose veins on the right leg. In addition, there was a large surface extending around the entire leg from the ankle to the upper third of the leg, somewhat higher in front than at the back, which had the appearance of the ordinary varicose ulcer of the leg, on an area of atrophy such as was described on the back of the left thigh. In the center, there were two healed ulcers and one open one, each about the size of a quarter. There was slight scaling of the lesions on arms and legs.

Subsequent Course.—The patient disappeared and was not again seen until February, 1921. During this time the condition had made distinct progress. There were several new ulcers, which had started after slight trauma. The telangiectases were less pronounced, but the petechial character of the lesions was more marked and in the larger lesion there were areas of uniform livid color. During examination, a slight accidental trauma caused visible cutaneous hemorrhage. Spots of reddish-brown pigmentation were appearing on the dorsum of the feet and toes. There were none on the soles or on the hands. The skin of the center of the large patch on the left thigh was thin, but closely adherent to the subcutaneous tissue, which had a hard sclerodermic feeling.



Fig. 6.—Distribution of lesions on back of body of patient in case reported by Dr. Ormsby.

At this time the urine was normal. The blood findings were: hemoglobin, 80 per cent.; erythrocytes, 4,704,000; platelets, 58,000; leukocytes, 9,400; large mononuclears, 75 per cent.; small mononuclears, 10 per cent.; eosinophils, 2 per cent.; basophiles, 1 per cent.; bleeding time, four minutes, coagulation time, seven and one-half minutes; sugar, 99 mg. per 100 cubic centimeters; urea, 14 mg.; nitrogen, 29 mg.

In this case, there was no edema of the eyelids, no leukoplakia-like patches in the mouth, and the face was not affected, all of which conditions have been found in several of the previously reported cases. On the other hand, there were ulcerations and large varicose veins of the legs, conditions not previously reported.

CASE 14 (Presented by Dr. Ormsby¹⁶ at the Chicago Dermatological Society, January, 1916).—*History*.—The patient, a man, aged 33, born in this country, consulted Dr. Ormsby, Jan. 13, 1916, concerning an indurated lesion involving the glans penis. This lesion had been present five months. It had been treated with silver nitrate and had slowly increased in size. Regional glandular involvement was noted. The general examination revealed the cutaneous disorder concerned in this report and was disconnected with the present lesion. The subsequent history of this lesion proved it to be a lymphosarcoma which became generalized by metastatic involvement of the abdominal and thoracic regions, terminating fatally in one year.

The peculiar pigmentary and atrophic cutaneous disorder had been present many years. The patient stated he had always had a peculiar skin. No subjective sensations were noted except smarting in cold weather when the skin was unusually dry. The family history was negative.

Physical Examination.—This revealed a rather obese young man, in good general health. The face, neck and hands were free from lesions. The scalp was normal and covered with thick normal hair. The trunk was covered with pigmented macules which varied in size from that of a small pea to areas larger than a silver half dollar. These were contiguous with each other producing a mottled effect. The lesions were yellowish brown and were slightly atrophic. The most marked areas occurred around the waistline under the belt. The arms and legs were similarly affected but less intensely pigmented. On the thighs were large areas of telangiectasia and atrophy strongly resembling healed radiodermatitis. Pigmentation was much less conspicuous in the thighs than elsewhere.

The patient was shown at the annual meeting of the Chicago Dermatological Society, in 1916, at which time Dr. Foerster, of Milwaukee, suggested the diagnosis of poikiloderma atrophicans vasculare from his recollection of a plate he had seen in *Ikonographia Dermatologica*. Other members agreed that such a case had not been seen by them.

Histology.—Four pieces of tissue were excised from areas presenting differing clinical pictures. The epidermis was well formed in most areas. Over certain areas in which collections of cells were present in the corium, the epidermis was thinned. The corium presented changes in the collagen, elastin and vessels.

16. Ormsby, O. S.: Case for Diagnosis, J. Cutan. Dis. **35**:42, 1917. (Case presented at the Chicago Dermatological Society, Jan. 18, 1916. Discussion by Drs. Pusey, Wile, Harris and Irvine.)

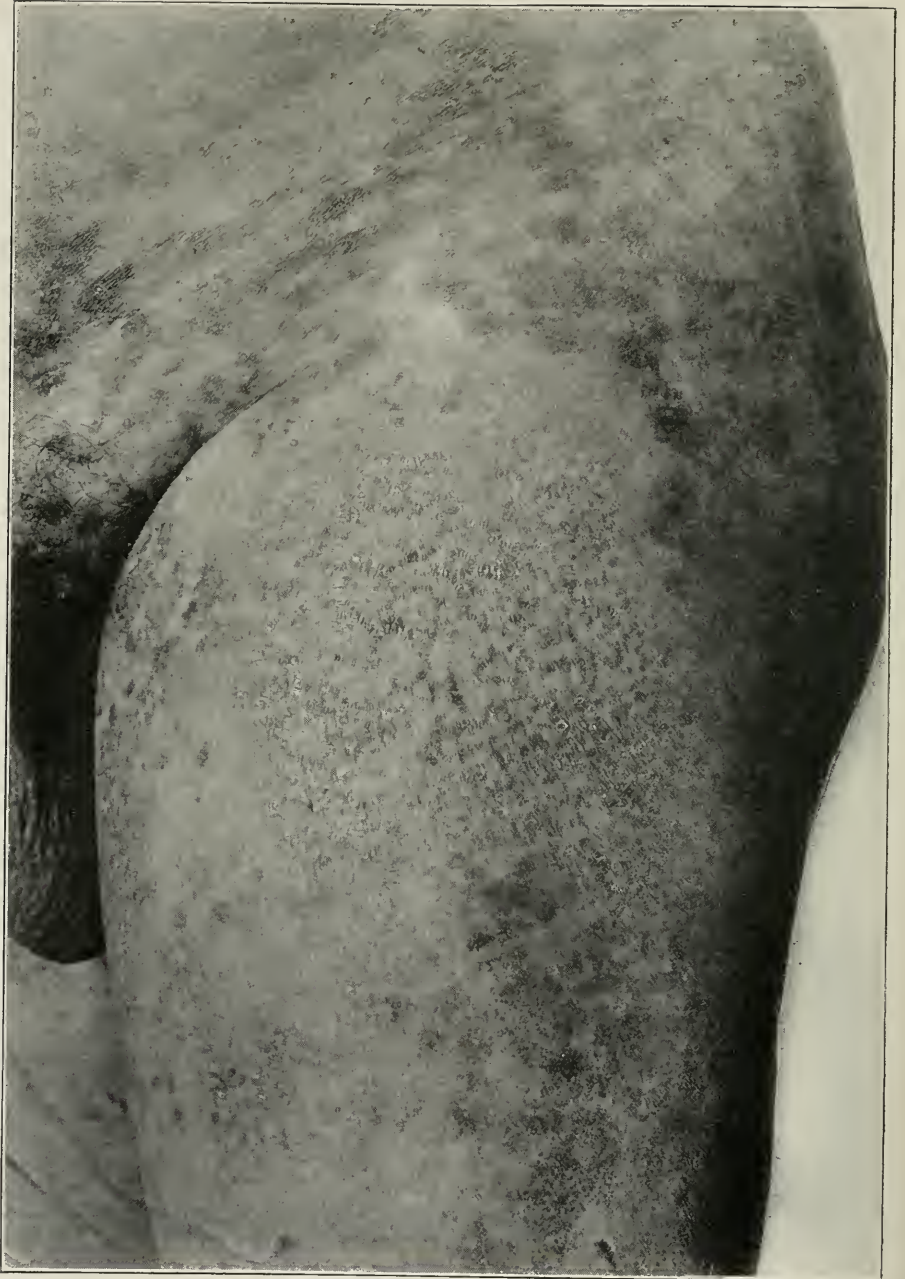


Fig. 7.—Lesions on thigh of patient in case reported by Dr. Ormsby.

There was much cellular infiltration, which occurred in groups, columns, about vessels and irregularly disseminated. The cells were round and oval, and of the connective-tissue type. The collagen stained poorly and presented evidences of degeneration. In some sections elastic tissue was absent, in others broken and irregularly placed. The vessels were dilated and in many areas surrounded by a cellular infiltration. Pigment was present in the corium in sections taken from clinically pigmented areas. This was apparently of blood origin. Some coil glands were present and a very few hair follicles and sebaceous glands remained. The histologic picture was therefore entirely unlike lupus erythematosus and presented the features common in cutaneous atrophy.

Four other doubtful cases have been reported.¹⁷

SUMMARY OF CASE REPORTS

Of the fourteen patients described, nine were male and five female. The youngest was six, two were 41, the rest were between 20 and 33. In all cases in which any reference to it was made, the Wassermann reaction was negative.

In a few cases, other diseases were found associated with the poikiloderma. These were: Tuberculosis of the lungs, myositis, rheumatic or gouty manifestations, juvenile muscular atrophy, calcareous deposits, malaria, ichthyosis, lymphosarcoma. Edema of the eyelids was present in several cases, and in one of these it disappeared while the patient was under observation.

Here is a small group of cases varying to a considerable extent in many of the minor manifestations, but remarkably similar in their main outlines. Accepting the nearly constant factors as characteristic, we have a complex, widely distributed dermatosis, beginning usually in late youth or early adult life, of very slow evolution and of approximately symmetrical distribution, attended by mild pruritus and presenting as its chief manifestations associated telangiectasis, pigmentation, and later, capillary hemorrhages and atrophy. It is frequently associated with a more or less transitory redness and edema of the eyelids, and with telangiectasis and leukoplakia-like lesions of the mucous membrane of the mouth. Its histology shows two stages, an

17. Scholtz: Ein beginnender Fall von Poikilodermie (?), Arch. f. Dermat. u. Syph. **117**:877, 1913-1914. (No reference to this case is made in this paper, as there was no description of it and no discussion. It was presented Oct. 13, 1913, at the Nordostdeutsche dermatologische Vereinigung); Janovsky, V.: Drei Fälle familiärer Hautatrophie (Poikiloderma Atrophicans), Arch. f. Dermat. u. Syph. **130**:388, 1921. (This article appeared after this paper was written. It describes three patients in one family, girls, aged 8, 10 and 12. The eruption, limited to the face, consisted of redness, yellowish pigmentation, seen with the diascopes, and small atrophic spots. The cases were of short standing, and there is some question as to whether they are poikiloderma.)

inflammatory and an atrophic. The inflammatory stage is manifested by perivascular round-cell infiltration, and dilatation of the superficial vessels and alternate increase and diminution or absence of pigment; the atrophic stage by flattening of the papillae, degeneration and disappearance of the elastic tissue, and atrophy of the collagen bundles.

GROUPING, DIAGNOSIS AND CLASSIFICATION

Most of the observers are agreed in grouping these cases together. There is, however, some doubt as to whether the case of Petges and Cléjat and Schramek's second case (Case 8) should be included in the group.

Jacobi believed that the condition was a disease, *sui generis*, not to be included in any group previously described. At the time of the presentation of Jacobi's case, Ehrmann¹⁸ was of the opinion that it was an erythema of toxic origin, having many analogies with scleroderma, which he attributes to a similar cause. Kreibich¹⁸ and Arndt¹⁸ considered it lupus erythematosus, pointing out that there was no sclerodermic thickening. Jadassohn¹⁸ replied that all the characteristics of lupus erythematosus were lacking, and agreed with Ehrmann in considering it to be scleroderma. He held to this view in his discussion of Müller's case⁷ and after the reporting of several later cases. In his notes to the German edition of Darier's *Précis de Dermatologie*, published in 1913,¹⁹ he classed the cases as atypical scleroderma. Jadassohn⁷ agreed, however, that it was wise to designate this group with a special name. By so doing, attention would be called to it, and if later it should be proved that the group represented transitional forms of some already well-defined disease, it could then be included in it. Scleroderma was a disease of varied symptomatology, its etiology was unknown and possibly complex, and poikiloderma was possibly related to it.

Darier did not accept Jadassohn's view and, in the second French edition of his book (1918), classed poikiloderma under the diffuse idiopathic atrophies.²⁰

Glück,⁸ grouped his own case with the rest, but thought that they should be classed as a subdivision of the group of idiopathic atrophies.

Brocq²¹ also provisionally classified poikiloderma under the diffuse idiopathic partial atrophies.

18. Quoted by Jacobi (Footnote 2).

19. Jadassohn, note in Darier, J.: *Grundriss der Dermatologie*, 1913, p. 244.

20. Darier, J.: *Précis de Dermatologie*, Ed. 2, 1918, p. 379.

21. Brocq, L.: *Précis-Atlas de Pratique Dermatologique*, Doin, Paris, 1921, p. 1097.

Müller²² classed Jacobi's, Zinsser's and his own cases as a variety of lupus erythematosus, calling them atrophoderma erythematoses reticularis. He distinguished a superficial and a deep variety, his own cases belonging to the superficial, the others to the deep variety.

Zinsser, in publishing his two cases, accepted Jacobi's view and classed his own cases with Jacobi's.⁴ In his discussion of Müller's case,⁷ he placed poikiloderma in the scleroderma group. This was also Weidenfeld's⁷ opinion.

Blaschko⁷ considered Müller's case a rare type of atrophying parapsoriasis. I have found nothing to support this opinion.

DISCUSSION

The evidence that the affection is lupus erythematosus is extremely weak, and, I think, may safely be discarded. In my case, there was certainly nothing to suggest that diagnosis to any one. Neither does the histology of the cases examined support it.

My impression is that it is not advisable at the present time to attempt any very definite classification of this group of cases, the number so far reported being too small for drawing final conclusions and for defining the limits of the disease. Furthermore, the classification of the sclerodermas and of the better known atrophies is still subject to revision. In addition to this, too few of the patients have been under observation sufficiently long for adequate study of the variations in the different cases. All the cases, except that of Petges and Cléjat, were of long standing when first seen, which may possibly account for the different pathologic findings in that case. The patient died of tuberculosis only two years after the beginning of the dermatosis. In a disease of this complexity, there of necessity must be considerable variation in the different cases, as well as at the different stages of development.

If it be necessary at present to place these cases in any general scheme, I should be inclined to adopt the suggestion of Glück, Darier and Brocq, which places them as a separate and fairly well defined group of the diffuse idiopathic atrophies, though I should be disinclined to dispute Jacobi's opinion that this condition may be a disease, *sui generis*.

Among the conditions which the different appearances of this group of cases resemble, without there being any possibility of confusion, are sunburn, healed roentgen-ray dermatitis, and angioma serpiginosum.

Other conditions which might possibly cause confusion and conceivably considerable difficulty in differentiation at some stages are: Schamberg's progressive pigmentary disease, Majocchi's disease, gen-

22. Footnotes 6 and 7.

eralized telangiectasia associated with syphilis, as described by Stokes, and purpuric erythema. Histologic examination would settle the point.

In the case of poikiloderma, shown by Civatte,¹² Queyrat called attention to the resemblance to the pigmentary changes in certain cases of syphilis, and in a case of purpuric erythema presented by Milian and Blum,²³ Darier pointed out the resemblance to poikiloderma.

When Ormsby's case was presented the resemblance to Majocchi's disease was noted by Pusey and Irvine, to healed roentgen-ray dermatitis by Pusey.¹⁶

When my case was presented, the resemblance of many of the lesions to healed roentgen-ray dermatitis was noted by all. The resemblance to angioma serpiginosum was remarked on by Whitehouse, Howard Fox, Highman, Wise and Winfield. Highman also pointed out the resemblance of some of the lesions to Majocchi's disease and to Stokes' case of specific telangiectasis.¹⁵

In most cases the differentiation between the pigmentary and the rare purpuric eruptions of syphilis should present few difficulties that could not readily be solved by clinical examination. If doubt still remained, the histologic examination would settle the question as the changes in syphilis are totally different from those of poikiloderma.

In purpuric erythema (frequently called symptomatic purpuric erythema), the purpuric lesions predominate, while in poikiloderma they are not always present, and when present they do not predominate till late in the disease, when there is no possibility of confusing the two conditions. In purpuric erythema, there is no itching, no edema and no atrophy and the disease is of rapid evolution and does not usually last more than three or four months, when it entirely disappears. Occasionally it recurs. In no case of poikiloderma so far reported has there been disappearance or even arrest of the progress before atrophy is reached. The presence of articular pains, the distribution of the eruption, and the pigmentation are points of resemblance.

In angioma serpiginosum there are usually no subjective symptoms (no itching), and there is no purpura. The extension of the disease is slow but it is usually not symmetrical. The elastic fibers of the skin remain normal.

In Schamberg's disease, pigmentation is the predominating sign, the eruption is not symmetrical and is usually not so extensive. There is very little, if any, atrophy. The epidermis is normal and there is a dense infiltration in the papillary and subpapillary layers.

The similar points in Majocchi's disease are telangiectasia, petechiae, atrophy of mild grade and the presence of rheumatic pains. In this

23. Milian, G., and Blum, P.: Erythème purpurique, *Bull. Soc. franç. de dermat. et syph.*, p. 272, 1919.

disease, too, the elastic fibers are atrophied or destroyed. It differs from poikiloderma in that while the eruptive period is of several months' or years' duration, the lesions eventually disappear. There is usually no itching, though occasionally it may be present. There is never edema, erythema or infiltration. It is usually limited to the legs, while the upper part of the body is the part most frequently affected in poikiloderma. The histologic examination shows dilated vessels, perivascular round-cell infiltration, peripheral endarteritis, hyalin degeneration of the intima, and atrophy of the hair follicles.

ETIOLOGY

Nothing is known of the etiology of poikiloderma.

Petges and Cléjat suggested that toxic bodies acting on the vessels and connective tissue may have played a rôle in the etiology, and Jacobi thinks that these toxic bodies may have been evolved by the tuberculosis which was present in their case, but absent in his. Erhmann, as already noted, also believes it to be of toxic origin.

Zinsser attributes his cases to a congenital disease about the smallest blood vessels, which were injured in early life by the trauma of cold on the most exposed parts of the body.

Glück is inclined to accept a common etiology for the various conditions found in his case, epilepsy, muscular dystrophy, calcareous deposits in the subcutaneous and muscular tissue and poikiloderma. He suggests, as the common etiology of this variety of lesions, a defect original in the germ cell.

Bettmann¹⁴ also is inclined to the theory of an embryonic defect, perhaps similar to those presumed to exist in late developing nevi—a disposition to poikiloderma—which furnishes a peculiar terrain on which extraneous influences cause the disease to develop. He states that this is an excellent field for speculation. The reader is referred to his article for the elaboration of this theory.

NOMENCLATURE

I have accepted the name given by Jacobi as sufficiently distinctive for this variegated dermatosis. This group of fourteen cases has already acquired four others. These are: *scélrose atrophique de la peau* (Petges and Cléjat); *poikilodermia atrophicans vascularis* (Jacobi); *atrophia cutis reticularis cum pigmentatione* (Zinsser); *atrophodermia erythematodes reticularis* (Müller); and *dermatitis atrophicans reticularis* (Glück).

ABSTRACT OF DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: I believe the disorder discussed by Dr. Lane is not an ordinary diffuse atrophy of the skin. All the men who saw his patient in Chicago agreed that the case was unique. The most striking thing

about it was the large number of patches that were exactly like healed radio-dermatitis. The atrophy, telangiectasis and pigmentation were typical. The termination of the patient's career was from a different disease altogether.

DR. HENRY H. HAZEN, Washington: I was much interested in this paper because I had a case of this sort in the office last fall, which I was unable to diagnose at the time. I am convinced from talking with Dr. Lane that the condition was the same, but the patient had gone on to a further stage. In addition, he had a syndrome which was extremely interesting. He had been a soldier and had been pretty well set up when he went into service. He had been in the hospital at Nashville. He first had muscular weakness, next loss of weight chiefly in the legs and arms, then the development of round shoulders and dropping of the abdomen. He then had loss of sexual power, marked loss of memory and, if I recall correctly, intense headaches, and lastly, he had nephritis. As he had been a worker in tar, the nephritis may have been due to that. He was sent to a number of internists and they were inclined to think there was a change in the pituitary gland.

DR. WILLIAM ALLEN PUSEY, Chicago: May I say just a word to endorse Dr. Pollitzer's suggestion that this be called "derma" and not "dermia," and enter a plea for that usage generally? In dermatology we get derma and dermia a good deal confused. It is hard to say how this termination has arisen. The correct word is derma. The only other derivation I can see is from the French "Dermie." Achilles Rose, a Greek physician, said he could find no reason for this termination.

DR. AUGUST RAVOGLI, Cincinnati: I was much interested and think the cases can be put together with the idiopathic atrophodermas. I had occasion some years ago to demonstrate a case of atrophy of the skin, I think unlimited, in a girl who died. She had congenital syphilis and at postmortem gumma was found in the brain. The case was very interesting. The skin on the whole lower half of the body was atrophic and just like tissue paper, or cigaret paper. The derma had nearly disappeared. In another case the skin on the back of the hand was red and shiny and then gradually became atrophic and the skin began to disappear, taking on the appearance of cigaret paper. There was a reticular appearance and some blood vessels like telangiectasia. I think they must have arisen from a neuritis, from a deep-seated affection of the central nervous system.

DR. FRED WISE, New York: I have seen only one case of this kind and it is difficult to speak with any great degree of intelligence about it, but what Dr. Lane said in reference to the classification of the disease interested me. I have read practically all the published articles, and if I may express an opinion, I think it cannot be classed with any other disease. It is certainly different from any other clinical entity and, as has been said, looks more like a healed roentgen-ray burn than any other condition. I think it is undoubtedly a disease entity and it is useless to class it with something else, because it resembles nothing else.

DR. SIGMUND POLLITZER, New York: As Dr. Lane has well said, the etiology of this class of case affords a fruitful field for speculation. It seems to me the entire picture of scleroderma and atrophoderma points decidedly to an endocrine disturbance.

DR. JOHN E. LANE, New Haven, Conn.: No studies of the basal metabolism were made, nor were roentgen-ray photographs of the pituitary taken. As Dr. Pollitzer has remarked, these might have proved of some value, but the patient was not a willing cooperator, and such studies as were made were carried on with the greatest difficulty. We should have liked to do many other things, but not even a biopsy was obtainable.

CLINICAL AND HISTOLOGIC FEATURES OF CERTAIN TYPES OF CUTANEOUS TUBERCULOSIS*

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NEW YORK

INTRODUCTION

Not only is the pathogenicity of certain forms of tuberculosis of the skin still the subject of lively debate, but even the clinical and histopathologic features of certain presumably tuberculous diseases have not as yet been definitely cataloged nosologically. Certain well-known diseases, of which lupus vulgaris and tuberculosis verrucosa cutis are prototypes, have, of course, been long recognized as being due to the invasion of the skin by the bacillus of Koch. As time went on, and investigations progressed, other skin diseases were soon proved to be of tuberculobacillary nature; among these are lichen scrofulosorum, acute disseminated miliary tuberculosis, scrofuloderma, tuberculosis ulcerosa and lupus miliaris disseminatus faciei. These diseases may be designated as "genuine" tuberculoses of the skin. Investigations carried on in recent years have resulted in the inclusion, in this group, of two closely related affections, namely, the erythema induratum of Bazin and the subcutaneous sarcoid of Darier. Still more recently, that is, within the last few years, this group has embraced also the so-called papulonecrotic tuberculids.

There still remains a large group of skin diseases, the tuberculous etiology of which is merely a matter of suspicion—a suspicion well grounded in relation to some affections, as in lupus erythematosus, lupus pernio, and Boeck's sarcoid—in other diseases as yet barely tenable, as in lichen nitidus, angiokeratoma, and certain forms of chronic exfoliating erythrodermas, as well as the pityriasis rubra of Hebra. It may well be that, in some not far distant future, some or all of these affections will be added to the group of tuberculobacillary diseases of the skin.

Of the various dermatoses mentioned, there are two interesting types of which the clinical and nosological status is not entirely free from elements of confusion. These are the papulonecrotic tuberculids (more especially the variety called acnitis) and lupus miliaris disseminatus faciei.

* From the service of Prof. John A. Fordyce, Vanderbilt Clinic, College of Physicians and Surgeons, Columbia University.

The following pages present a brief survey of the clinical, histologic and pathogenetic features of these two affections, including various data which are based on the more recent investigations in this field of dermatology.



Fig. 1.—*Lupus miliaris disseminatus faciei*: M. W. (Vanderbilt Clinic No. 5194, Feb. 7, 1919, Biopsy No. 727) woman, colored, aged 38, born in the United States, married but had never had any children. Family history, negative. As a child, she had had measles, whooping cough and chickenpox; and in later life typhoid fever. She had a persistent cough, and had lost 17 pounds within a little more than a year. The eruption appeared three years ago in the right ala of the nose, spreading to different parts of the face a year later. There were a half-dozen groups of dull purplish, smooth, firm, and sharply defined non-itchy lesions. On the nape of the neck there were about three dozen small pinhead-size, follicular, shiny lesions. (Courtesy of Dr. Howard Fox).

LUPUS MILIARIS DISSEMINATUS FACIEI

Lupus miliaris disseminatus faciei was first described by Tilbury Fox under the name "disseminated follicular lupus." As the lesions frequently show no relation whatever to the follicles of the skin, the latter name has been discarded in favor of the former.

The affection is a "true" tuberculosis of the skin, in the same sense as lupus vulgaris. It should not be confounded with the postexanthematic acute disseminated miliary tuberculosis of the skin. The latter is a grave and often fatal manifestation, which may accompany general miliary tuberculosis; the former is a benign dermatosis, characterized by an almost invariable predilection for the face and neck. Nor should it be confounded (as it so often is, even by those having considerable training and experience) with Barthélemy's "acnitis," the deeper of the two forms of papulonecrotic tuberculids, with its site of predilection on the face.¹

Clinical Features.—Lupus miliaris disseminatus faciei presents these characteristic features:

The lesions appear in the course of several weeks or months, often occurring in crops, almost always breaking out on the face, and rarely invading the hairy scalp. Sometimes lesions appear sparsely on the neck, and sometimes on the nasal mucosa, but more often they appear on the labial mucosa. Occasionally, an acute hyperemia precedes the outbreak, the lesions becoming manifest after the redness has subsided. The lesions consist of flattened, or slightly elevated, pinhead to bird-shot sized papules of rounded or oval form, at first bright red and later brownish red. Diascopic pressure does not always demonstrate the yellowish-brown tint of lupus (Jadassohn).² Pressing the papule with the point of a toothpick reveals the soft consistency of lupus tissue; the lesion may be readily curetted out of the skin en masse. There is usually no tendency toward peripheral enlargement, nor to ulceration, tumor formation, or confluence of individual lesions. Lesions have been described showing central elevations, shrunken follicular orifices, milium bodies, and little "yellow spots." Papules capped by tiny pustules and crusts have been noted; suppuration and caseous degeneration may occur, although the latter changes may in some instances represent those of an ordinary concomitant acne vulgaris. The individual papules may persist over long periods, finally to shrink and disappear, while fresh crops may break out after long or short intervals. After curettage, recurrence may take place at the edge of

1. The superficial form of papulonecrotic tuberculid, Barthélemy's "folliclis," occurs most frequently on the backs of the fingers and hands, sometimes on the palms also, the ulnar aspect of the forearms, about the points of the elbows, and on the lower extremities and the trunk.

2. Jadassohn: In Mrazek's Handbook of Skin Diseases, 4:272, 1907.

the scar. Aside from occasional moderate itching, subjective symptoms are absent.

The eruption may accompany other evidences of manifest visceral tuberculosis, or it may attack an individual who has no other signs of tuberculosis. Rarely, an eruption of acnitis papules, or acnitis of the face and erythema induratum of the legs, may coexist with the lesions



Fig. 2.—Lupus miliaris disseminatus faciei: A. S. (Vanderbilt Clinic No. 24138, Sept. 2, 1919, Biopsy No. 791) man, Italian, married, aged 26. Duration of eruption, about 6 months. Scattered over both cheeks and the forehead were about fifty pinhead- to lentil-size, semitranslucent, firm nodules, conical in shape and elevated well above the surface of the skin. The color was a pale brownish-red. Many of the lesions had undergone a central dry necrosis and were capped with a crust. Note the agminated papules at the root of the nose.

of disseminated miliary tuberculosis (Jadassohn).² There may be a coexisting rosacea.

Histopathology.—As a rule, microscopic examination of a papule reveals a typical tuberculous structure, usually with caseous degen-



Fig. 3.—Lupus miliaris disseminatus faciei: E. S. (Vanderbilt Clinic No. 1624B, May 26, 1920) woman, colored, aged 20, married, "presented lesions on the neck and face, of one year's duration. On the back of the neck there were from fifteen to twenty lichenoid papules, flat and shiny, some umbilicated, varying in size from a pinhead to a lentil, and having the consistency of a keloidal acne. Slight depigmentation was present on the surface of the papules. Around the nose on both lips, and on the upper eyelids there were closely crowded millet-seed size papules; also in this location and on the nose and chin were a few flat, papular lesions, varying in color from a dark purple to a light brown. The smaller lesions on the nose resembled lupus vulgaris in color and consistency." (Courtesy of Dr. Isadore Rosen).

eration.³ The tubercles, only some of which bear a topographic relationship to the follicles, are usually sharply defined, with a moderate or more extensive zone of lymphocytic infiltrating cells. The larger areas, more especially, show advanced caseation. In the center of a



Fig. 4.—Lupus miliaris disseminatus faciei: E. G. (Vanderbilt Clinic No. 16561, June 6, 1919, Biopsy No. 773), woman, aged 23, born in the United States, single. She presented an eruption consisting of a number of pinhead-to birdshot-size oval and rounded lesions, scattered over the face, but most pronounced on the vermillion border of the lips and about the canthi of the eyes. The papules were soft and somewhat translucent, some of them having a small central depression. She was treated for a "metastatic choroiditis" of the right eye at the Knapp Memorial Hospital. Duration of eruption, about one year.

3. Compare this with the usual histopathologic appearance of papulonecrotic tuberculids, especially acnitis.

caseated area, Brinitzer and Lewandowsky⁴ observed the distinctly outlined elastic wall of a venule. According to Delbanco, the tuberculous infiltration has its origin in the adventitia of the small arteries and veins.



Fig. 5.—Papulonecrotic tuberculid: folliculitis, acnitis and lupus erythematosus. Y. J., aged 13; the diffuse patch covering the nose is indistinguishable from lupus erythematosus. The cheeks present a typical "acnitis," the arms and hands a typical "folliculitis," together with pernio of the fingers. (Vanderbilt Clinic).

4. Lewandowsky: *Die Tuberkulose der Haut*, Enzyklopaedie der klinischen Medizin (containing a complete bibliography), Berlin, J. Springer, 1916.

In the opinion of Jadassohn² there is no doubt as to the tuberculous nature of the eruption. The histopathologic changes point to a hematogenous infection, although cases have been reported in which no other focus of tuberculous infection could be discovered (Kraus,



Fig. 6.—Papulonecrotic tuberculid: W. P., a child afflicted with congenital syphilis; showing agminated papulopustular lesions, involving most of the skin at different periods. This type of eruption is sometimes called "acne scrofulosorum." (Vanderbilt Clinic).

Hoffmann, Loewenberg, Rusch and others). Patients with a coexisting phthisis have been reported by Arndt, Briinitzer, Bruusgaard, Oppenheim, and several other observers.

Pathogenesis.—The disease is a relatively benign bacillary tuberculosis of the skin. Tubercle bacilli, in several instances, have been demonstrated in the lesions, in both smear preparations (Bettmann, Arndt, Schlasberg) and in sections of tissue (Finger, Arndt). Animal



Fig. 7.—Papulonecrotic tuberculid: J. M., showing "acnitis" papules of face. (Vanderbilt Clinic).

inoculations were successful in the hands of Favera, Hoffmann, Jadassohn,² and Kyrle. Positive focal tuberculin reactions were noted by Jadassohn,² Bettmann, Cohn and Opificius, Favera, Finger, Kraus,

Kryle and Werther. General reactions were seen by Delbanco, Loewenberg and Schlasberg. Successful therapy with tuberculin injections is recorded by Delbanco, Kraus and Mucha. The von Pirquet test is usually positive.

In short, the demonstration of the bacillus of Koch in the lesions, the positive animal inoculations, and the occurrence of focal tuberculin reactions leave little doubt as to the bacillary nature of the dermatosis. Negative findings must be relegated to a place of secondary importance.

Coexistence of Lupus Miliaris Faciei and Acnitis.—The coexistence of lupus miliaris disseminatus faciei and acnitis of the face has been



Fig. 8.—Papulonecrotic tuberculid: J. I. (private patient, Dr. Wise), showing the typical papulonecrotic lesions and scars left by former lesions. This young man had "acnitis" of the cheeks.

noted by Arndt, Bettmann, E. Hoffmann and Török. Jadassohn,² on several occasions, mentioned the coexistence of the two forms of eruption. Schamberg,⁵ on the other hand, doubts that a clinical differentiation can be made between them. Zieler⁶ emphatically says, "There is no doubt that acnitis is clinically different from disseminated miliary lupus of the face." This is an opinion with which we are in accord.

5. Schamberg, J. F.: A Study of Acnitis with Report of an Extensive Case, *J. Cutan. Dis.* **27**:14, 1909.

6. Zieler: Die Tuberkulose der Haut, in Jesionek's *Haut und Geschlechtskrankheiten*, 1914.

In the accompanying table, the salient features of the two affections are compared.⁷

COMPARISON OF ACNITIS AND LUPUS MILIARIS DISSEMINATUS FACIEI

Acnitis	Lupus Disseminatus Faciei
Relatively common	Relatively rare
Attacks the face, but is rarely seen on the mucosae of the lips and the nostrils. There is often a coexisting eruption of "folliclis" on the upper extremities, and sometimes on the trunk and lower limbs	Almost always limited to the face, with a few lesions on the neck: predilection for mucosae of the lips and the nares, and the skin of the eyelids
The lesions are papulonecrotic, and usually numerous	The lesions are smooth and shiny: rarely show tendency to central necrosis. Relatively sparse
Applejelly color absent	Applejelly color usually seen
Associated acro-asphyxia and perionies of the fingers very common	Absent
Coincident eruption of lupus erythematosus, erythema induratum, Darier's sarcoid, etc., often observed	Absent
Histologic structure usually that of an ordinary inflammatory reaction Occasional tuberculoid structure encountered	Histologic structure that of a tuberculoma, usually with central caseation
Tubercle bacilli rarely detected	Tubercle bacilli found with relative frequency

Lesions of acnitis and lupus miliaris disseminatus faciei may coexist, although rarely.

THE PAPULONECROTIC TUBERCULIDS

Whereas disseminated miliary lupus is a comparatively rare affection (at least in this country), the incidence of the papulonecrotic tuberculids is a relatively common one. It would be superfluous to enter here into a detailed discussion of their symptomatology; everyone is familiar with the pictures described by Barthélemy under the titles "folliclis" and "acnitis."⁸ It is conceded by the majority of the prominent workers in this field that these are two more or less similar clinical manifestations of one and the same dermatosis.

Folliclis is the more superficial form. It appears most frequently on the backs of the fingers and hands, on the palms at times, on the

7. Practically all American textbooks describe acnitis and lupus miliaris disseminatus faciei under the same heading. Some authors do not even differentiate the two types of eruption.

8. The case described, by Knowles, for example, (*J. Cutan. Dis.* **35**:61 [Feb. 17] 1917) as "Acnitis in the Negro" corresponds with the modern conception of lupus miliaris disseminatus faciei, both in its clinical and its histologic features.

ulnar surfaces of the forearms, and about the points of the elbows. It often, however, attacks also the skin of the trunk and of the lower extremities.

Acnitis is the deeper form, affecting chiefly the face.

The eruption on the hands is frequently associated with pernioles of the fingers, or merely with acro-asphyxia, and with an eruption of facial lupus erythematosus. Occasionally one sees patients exhibiting a variety of dermatoses at the same time: for example, papulonecrotic tuberculid and lupus erythematosus of different parts of the body; tuberculid and erythema induratum; tuberculid and sarcoid; tuberculid and scrofuloderma, etc. These combinations are, of course, strongly suggestive of the tuberculous pathogenicity of what Darier called the tuberculids, and Lewandowsky⁴ now calls "tuberculosis papulonecrotica."



Fig. 9.—Papulonecrotic tuberculid: showing a typical isolated palmar lesion of "folliclis" (Vanderbilt Clinic). Palmar lesions of folliclis are comparatively uncommon. They leave irregularly stellate pits.

Pathogenesis.—For many years the subject of spirited controversies, the pathogenesis of these eruptions is still a partly unsolved problem. Wolff-Eisner defined the tuberculids as "local reactions wherein nature has set up a cutaneous reaction, which indicates the response of the skin to the products (or derivatives) of tubercle bacilli." While

Zieler⁶ regards them as "reactions of cutaneous hypersusceptibility in tuberculous individuals, provoked by disseminated tubercle bacilli, these reactions as a rule leading to the destruction of metastasizing tubercle bacilli."

The theory that the lesions are provoked by the toxins of tubercle bacilli was favored strongly by Boeck, Hallopeau, and Klingmueller. Later, Jadassohn,² Zollikofer, Darier, and Haury advanced the hypothesis that the tuberculids were provoked directly by tubercle bacilli; but that these occurred as attenuated, broken down, or dead, organisms. Jadassohn² believed that at some time in the course of their evolution, the lesions harbor tubercle bacilli, but that these are destroyed by the natural immunity processes of the affected individual. There is no doubt that various immunity processes and allergic phenomena play a very important part in the pathogenesis of these dermatoses.

The modern conception postulates the existence of a hematogenous tuberculous infection. It is presumed that the lesions result from the activity of isolated tubercle bacilli, occurring in scant numbers in the skin. The bacilli circulating in the blood stream ultimately find a resting place in the blood vessels of the cutis, there to be subjected to the action of various antibodies, finally undergoing lysis, and liberating certain toxins, which presumably play a part in the formation of the papulonecrotic lesions.

According to Roemer and Lewandowsky,⁴ their experiments on guinea-pigs tend to show that antibodies are potent not only against infections with foreign organisms, but also against their own virus. They assume that the tubercle bacilli provoke so-called "reactions of hypersusceptibility" in the skin, and are themselves destroyed in loco, thus explaining the difficulty in finding tubercle bacilli in the lesions of folliclis and acnitis.

The tuberculobacillary nature of these eruptions has, however, been established in several instances. Successful animal inoculations were reported by Philippon and later by Burnett. In sections studied by MacLeod and Ormsby, a typical tuberculous structure was encountered, together with two tubercle bacilli. The bacilli were found in sections of tissue by Whitfield and by Bossellini, using Ziehl's stain. Hidaka demonstrated the organisms by the antiformin method. In the papulonecrotic tuberculids of children, Leiner and Spieler obtained positive findings in a series of cases, both microscopically and by animal inoculations. Leiner inoculated guinea-pigs with material obtained from a "folliclis" papule, infecting the animals with tuberculo-sis. Lesions were examined microscopically by Gougerot and Laroche, who found in them no evidence of a tuberculous structure; and yet

material from these lesions, when injected into guinea-pigs, yielded tuberculous lesions in the animals, in which Gougerot demonstrated tubercle bacilli.

Positive focal tuberculin reactions have been frequently reported, following subcutaneous injections of tuberculin (Ehrmann, Jadassohn,² Hoffmann, Juliusberg, Zieler,⁶ and others). The transition of tuberculids into general miliary tuberculosis of the skin has been noted on several occasions.

E. Hoffmann observed a patient who presented an eruption of tuberculosis verrucosa cutis together with a papulonecrotic tuberculid; and apparently some of the latter lesions seemed to "develop" from the former. Bloch reported a similar clinical instance in a patient convalescing from measles. In such cases the verrucous tuberculosis is probably due to "metastasizing" tubercle bacilli, while the tuberculids might be attributed to the action of toxins. Zieler,⁶ however, believes



Fig. 10.—Papulonecrotic tuberculid: Showing the active papulonecrotic lesions of "folliclis"; depressed, sharply outlined white scars from earlier lesions. The area of predilection, the ulnar surface of the forearm, is well shown here. (Vanderbilt Clinic).

that varying grades of immunity play no part in these manifestations, but that they depend merely on larger or smaller masses of "metastasizing" tubercle bacilli, finding lodgment in the skin. Juliusberg observed a lupus nodule developing in a folliclis scar, and demonstrated the lupus tissue microscopically. MacLeod speaks of crops of acutis becoming "transformed" into lupus vulgaris. Darier and Brissay reported the development of lichen scrofulosorum in the scars of folliclis. Alexander published the report of a case which exhibited, first, an outbreak of multiple verrucous tuberculosis, followed some time later by an attack of papulonecrotic tuberculids. Bloch, Leiner and Spieler, and others report the occurrence of tuberculid eruptions subsequent to acute infectious diseases, more especially measles.

The appearance of tuberculids in infants and young children points to the existence of visceral tuberculosis, and is therefore of grave significance, especially as the cutaneous eruption is often the first manifestation of the infection and hence, may be a valuable warning signal. The concomitance of cutaneous tuberculids and phthisis, tuberculous adenitis, and other manifestations of visceral or bone tuberculosis is quite common.

It is conceded by most authorities that one of the probable reasons for the frequent negative findings lies in the paucity of demonstrable tubercle bacilli lodging in the lesions which are utilized for examination and inoculation experiments. It is necessary to make use of many lesions in different stages of development, and showing different phases of evolution, for purposes of laboratory investigation. In this country, it is especially difficult to induce patients (most of them being ambulatory dispensary cases, and in good general health) to part with more than one or two little bits of their cutaneous envelopes for purposes of scientific investigation. All investigators who have had much experience in this field of laboratory work emphasize the need for the utilization of far more abundant material in the bacteriologic and inoculation experiments in this group of eruptions.

The clinical and laboratory data are sufficiently suggestive to justify the assumption that the papulonecrotic tuberculids—despite their frequent nontuberculous histologic structure—are also forms of true tuberculosis of the skin: tuberculosis papulonecrotica.

Coexistence of Acnitis and Folliclis.—Among the more modern writers there is a growing tendency to regard folliclis and acnitis as so closely related nosologically that the same interpretation of their pathogenesis is applicable to both types of eruption. Folliclis has been the subject of much more extensive and detailed investigation than has acnitis; the probable reason for this being that folliclis is more common, and, occurring on the hands and arms, lends itself more readily to biopsy procedures than does the facial acnitis. While there seems to be a practically unanimous agreement as to the tuberculobacillary nature of folliclis, the same unanimity of opinion does not obtain with regard to acnitis. Barthélemy, for example, consistently denied the identity of the two eruptions. Jadassohn does not commit himself, but holds that the tuberculous origin of acnitis still remains to be definitely demonstrated. The consensus of opinion is that, while folliclis is always a tuberculobacillary disease, acnitis may at times be a tuberculous manifestation, at other times a nontuberculous—very much as is, presumably, the case with lupus erythematosus. However that may be, the clinical observer cannot ignore the patent fact that *a majority of patients presenting the papulonecrotic lesions of folliclis on the upper extremities, have also a coexisting papulonecrotic eruption on the face.*

Histopathology.—Histologically the lesions exhibit very few typical changes, whether the tissue is obtained from fresh or from old papules. Most of the sections show merely the ordinary alterations which characterize inflammatory tissue, namely, cell infiltration, consisting of numerous round cells and few plasma cells. These infiltrates, occurring frequently about the sebaceous and sweat glands, undergo a slow process of necrosis. Involution takes place after spontaneous extrusion of the broken down central mass; the lesion heals, leaving a deep,

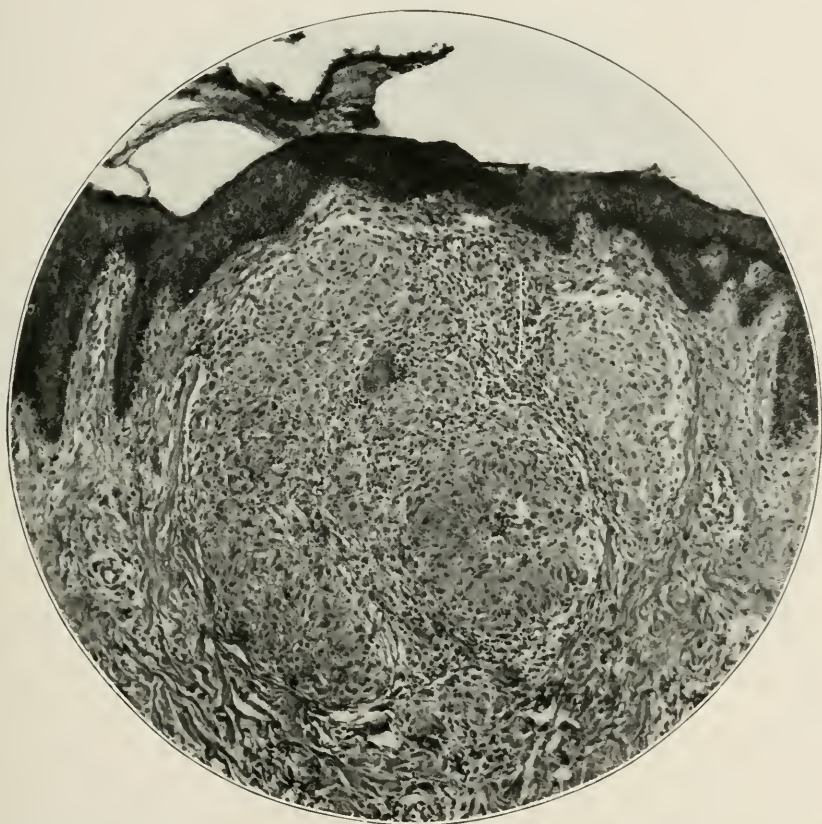


Fig. 11.—Lupus miliaris disseminatus faciei: biopsy material obtained from M. W. (Fig. 1); high power; showing the typical tuberculous nodules and a moderate number of round cells between the nodules

sharply defined round scar, often surrounded by a zone of pigmentation. On the other hand, the presence of epithelioid and giant cells has been observed by several investigators (Whitfield, Bossellini, Bunch, Gougerot, Haslund, Juliusberg and others). Tuberculous and "tubercloid" changes have been described (Darier and Walter, Herxheimer, Leiner and Spieler, MacLeod and Ormsby, Nobl, Philippon and Urban).

In connection with these atypical and aberrant histologic changes, Jadassohn² has aptly said: "In lepra and in syphilis, we find, beside the so-called 'characteristic' structure, also ordinary inflammatory and tuberculoid changes. Due to our limited knowledge, we have accustomed ourselves to regard only the most usual type of tissue reaction as being typical of a certain disease, and even to consider only such a 'typical' structure as being essential to diagnosis."

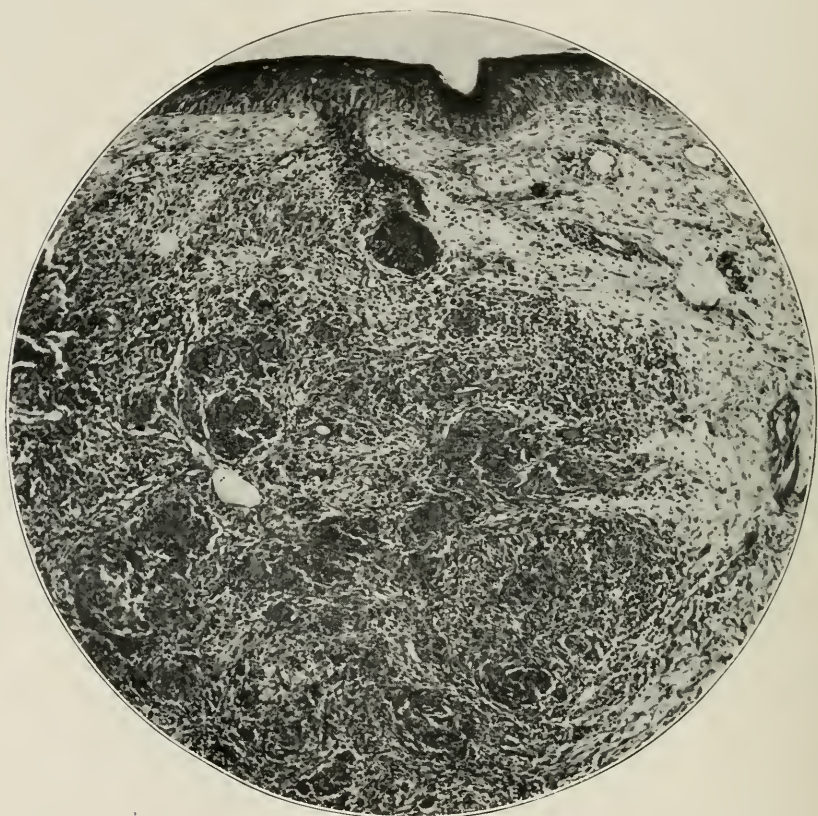


Fig. 12.—Lupus miliaris disseminatus faciei: biopsy material obtained from A. S. (Fig. 2); high power; showing a typical granuloma nodule—tuberculous tissue; subacute inflammatory reaction in the corium.

Briefly stated, it may be said of the papulonecrotic tuberculids, that in the present state of our knowledge, the clinical diagnosis carries with it far more weight than the histologic.

GENERAL HISTOPATHOLOGY OF THE PAPULONECROTIC TUBERCULIDS

According to Lewandowsky,⁴ the simplest histologic change in the papulonecrotic tuberculids—as is the case in all other hematogenous tuberculoses of the skin—consists of a circumscribed infiltrate of tuber-

culoid structure in the cutis. Very often the microscopic appearances present little or no evidences of a tuberculous structure, *the usual findings being those corresponding to an ordinary inflammatory reaction in the skin.* But those investigators who have had the opportunity to examine a large number of sections, obtained from various types of lesions, have on numerous occasions demonstrated in the cutis many small areas containing large giant cells of the Langhans' type, together



Fig. 13.—Papulonecrotic tuberculid ("Folliclis"); biopsy material obtained from L. B., No. 520, forearm; low power; showing simple inflammatory tissue; perivascular infiltration in upper, mid and deep cutis; moderate edema; necrotic area involving upper cutis and epidermis. Perivascular infiltration composed of lymphocytes.

with collections of epithelioid cells, so suggestive of tuberculosis. The most characteristic feature, however, is the necrosis. Small areas of necrosis may occur in any portion of the cutis, the surrounding tissue exhibiting a narrow band of epithelioid cells and lymphocytes. Such areas of necrosis are often observed in the upper portion of the corium.

just beneath the epithelium, the latter then taking part in the destructive process. The nuclei of the deeper epithelial cells take the stain poorly. Over the area of necrosis, there may remain only one or two layers of flattened, parakeratotic cells; or this portion of the epithelium may present a small, flattened vesicle, lying between the horny layer and the rete, and filled with leukocytes and cell detritus. Sometimes this vesicle will communicate with the subepidermal infiltrate, in which case an

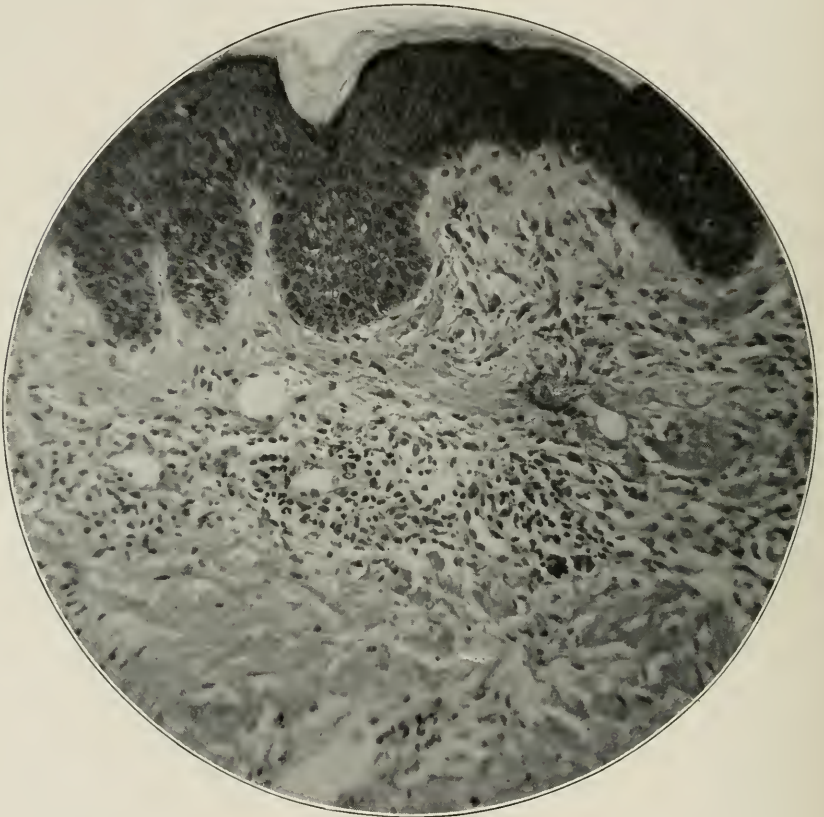


Fig. 14.—Papulonecrotic tuberculid ("Folliculitis"): biopsy obtained from A. P., No. 707, forearm; high power; showing the dilated vessels and perivascular infiltration of lymphocytes.

appearance similar to that of a furuncle is seen, more especially in the acneform tuberculids. The little abscess mass is composed of polymorphonuclear leukocytes and cell detritus; but at its periphery there are numerous epithelioid cells and sometimes also giant cells.

On either side of the necrotic area, the epithelium shows evidences of proliferation, with edema, hyperkeratosis and parakeratosis of the epidermis.

The necrosis may appear in any portion of the corium, down to the subcutis, and may be accompanied by lymphocytic tuberculoid infiltrates. The histologic structure of the superficial "folliclis" and the deeper "acnitis" is practically the same. In acnitis, the necroses are usually more widespread and are surrounded by a broad band of lymphocytes and epithelioid cells, with a few isolated giant cells. Within the infiltrates, the elastic fibers and normal collagenous bundles are wanting.

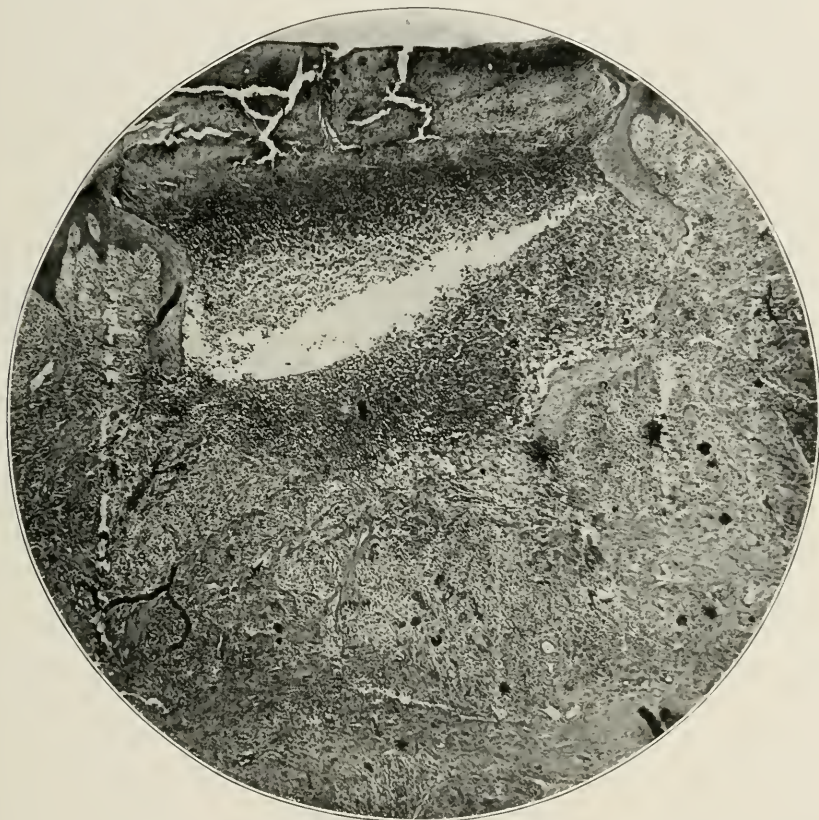


Fig. 15.—Papulonecrotic tuberculid ("Acnitis"): biopsy obtained from G. W., No. 440, face; low power; showing follicular necrotic plug; simple inflammatory tissue throughout cutis.

The infiltrates are located mainly about the deeper vessels in the region of the sweat glands, so that the latter are also implicated in the process, finally undergoing necrosis. This involvement of the sweat apparatus induced the older investigators to describe the process as though it began in these appendages of the skin. Further study has shown that these changes in the sweat glands are of secondary character.

The changes in the blood vessels constitute the determining factors in the pathogenesis of the tuberculids. Primarily, the deeper veins of the cutis are involved in the process, which begins as an endophlebitis with proliferation of the intima and thrombus formation, after which the necrosis appears. At first, there is a marked increase in the endothelial cells, until complete occlusion of the lumen takes place. The media and adventitia are thickened and studded with dense infiltrates, the latter forming perivascular mantles about the large and small vessels, following them for a considerable distance. Changes in the arteries also have been described (A. Alexander, Kren, Werther). These consist of an endarteritis, going on to complete obliteration, together with mesoarteritis and periarteritis. Werther believes that the whole process is due to an occlusion of the arteries, with its resultant structural changes. Jadassohn² and Lewandowsky⁴ have shown that both the veins and the arteries are involved in the process, as they are in other haematogenous dermatoses, but more so in the tuberculids than in other affections of the skin. According to most of the investigators, the occurrence of the necroses is directly dependent on the widespread endarteritis and endophlebitis affecting the vessels of the cutis.

It is possible, as Barthélemy suggests, that subcutaneous lesions like those of acnitis may exist, provoked by agencies other than the bacillus of tuberculosis. Those lesions manifest themselves as small, round, subcutaneous nodules, which, appearing without a coincident eruption of superficial papulonecrotic lesions, are difficult to identify clinically. However that may be, such subcutaneous nodules are most frequently encountered in association with the superficial papulonecrotic lesions; they may be interpreted as an expression of an embolic tuberculous process occurring in the deeper layers of the cutis.

COMMENT

Until 1910, Loewenberg found only thirty cases of lupus miliaris disseminatus faciei in the literature. Up to 1914, Lewandowsky⁴ found records of fourteen additional cases, making a total of forty-four. As a matter of fact, not a few instances of the eruption have been reported under the erroneous heading of "acnitis," so that the incidence of the disease is probably higher than these figures indicate. On the other hand, the papulonecrotic tuberculids are so common that a comparative numerical record is hardly considered of interest.

There is no doubt that certain examples of the dermatosis are not easy to identify clinically. Several authors mention instances in which the skin of the face exhibits, beside the typical smooth, shiny, yellowish papules, deepseated nodules like those found in cases of acnitis; hence

there is to be considered the possibility of a transition from one disease to the other, or, as already mentioned, a combination of both. But, in the typical eruptions, the individual papules are readily recognizable as small lupus formations, presenting a more or less definite applejelly tint, with sharply defined edges, and of soft consistency.

Recent Views as to Pathogenesis.—A series of experiments carried out by Gougerot and Laroche, involving many animal inoculations with papulonecrotic tuberculids, led them to advance certain hypotheses regarding their pathogenesis. They believe that the tuberculids are provoked by the effect, *in situ*, of casual isolated blood-borne (metastasizing) tubercle bacilli, together with their soluble and insoluble products. Tubercle bacilli of diminished virulence may give rise to similar but less characteristic changes in animals infected with tuberculosis, while dead bacilli probably have no (local) effect in such animals. The tuberculids manifest themselves only in animals with normal or increased resistance, not in those with diminished resistance. They summarize their findings as follows: The tuberculid is the outcome of a struggle between a bacillary embolus and an already sensitized soil in a state of semi-immunity. The metastasizing of tubercle bacilli is therefore a *conditio sine qua non*.

Zieler⁶ assumes that the tuberculids are caused by a "reaction of hypersusceptibility," manifested in the organism (i.e., tissue) in which an immunity already exists and in which the reaction is brought about by the agency of blood-borne tubercle bacilli. These cause a marked reaction in the presence of the specific "irritability" of the tissues. This reaction may lead to a destruction of the infectious material, or, possibly, only to an inhibition of its powers of regeneration (multiplication). Assuming this to be the case, one may eliminate the conception of a tuberculid resulting from the dissemination of a virulent or dead bacterial material. The tubercle bacilli may be very virulent and, as Török has shown by animal experiments, they may be as virulent as those in the primary focus which was their source. Zieler⁶ believes that the tuberculids are comparable, after a fashion, with the superinfections, in which the causative organism may be either destroyed, or may be rendered harmless without being destroyed or losing its virulence, through the active reaction of the allergic skin, i.e., through a cellular reaction.

SUMMARY

Of the various forms of disseminated tuberculosis of the skin, the clinical and histopathologic features of two different types have been recapitulated: namely, lupus miliaris disseminatus faciei, and the papulonecrotic tuberculids.

In dermatologic literature, the two affections are not infrequently confused. However, they represent entirely different clinical and histopathologic entities.

While the pathogenesis of lupus miliaris disseminatus faciei is probably identical with that of other forms of lupus, there is still much to be learned with regard to the pathogenesis of the papulonecrotic tuberculids.

In the light of present day knowledge, and as a result of numerous experiments and investigations, it is justifiable to assume that the latter affection, as well as the former, is of tuberculobacillary nature: i.e., tuberculosis papulonecrotica.⁹

9. In addition to the references already given, the following will be found of interest: Fordyce, J. A.: Histological Studies in Some Types of Skin Tuberculosis, *J. Cutan. Dis.* **32**:23, 1914; Low, R. C.: Tuberculids and Their Relation to Tuberculosis of the Skin and Other Organs: A Critical Review, *Edinburgh M. J.* **24**:114 (Feb.) 1920; Ketron, L. W.: Report of a Case of Acnitis with a Study of the Point of Origin of the Pathologic Process, *Bull. 20, Johns Hopkins Hosp.* **26**:111, 1915; Wise, Fred: Miliary Tuberculosis of the Skin, *Lichen Scrofulosorum and Papulonecrotic Tuberculids*, *J. Cutan. Dis.* **37**:105 (Feb.) 1919.

XXV.—DARIER'S DISEASE IN THE INFANT*

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ST. LOUIS

In 1889, Darier brought to our attention an unusual skin manifestation which was characterized by the occurrence of a follicular keratosis with a peculiar histopathologic picture, a more or less generalized distribution and associated lesions of the mucous membranes. Since then many cases similar in all respects to this original description have been reported, most of them however having been observed in young or old adults, a search through the literature revealing no detailed description of its onset in an infant. This case seemed to be of interest, not only because of its skin picture and early presentation, both as to age and date of onset, but particularly because of the presence of unusual mucous membrane lesions.

REPORT OF CASE

History.—R. S., a male child of 27 months, born of American parents on a farm in southern Illinois, was first seen at the office of Dr. M. F. Engman on Jan. 6, 1921, and referred to the Barnard Free Skin and Cancer Hospital two days later. He remained under hospital observation for forty-seven days, since which time he has been seen at weekly intervals to date of report.

The patient was the third of four children; the first and last children were healthy and apparently normal in every respect; the second child died two hours after birth of an unknown cause. The father and mother were healthy, and the family history as far back as it was possible to learn was negative to tuberculosis, syphilis and diseases of the skin.

The father states that the child, born of an uneventful labor and weighing 7 pounds, had been very well nourished and free from disease until ten months previous to presentation at our clinic. At that time the child had an acute tonsillitis with presumably a peritonsillar abscess which ruptured three or four days after the onset of illness. Concurrently a discharge from the ear became noticeable. About four months after the occurrence of these symptoms an eruption was seen over the upper portion of the back. This spread slowly in all directions and within three weeks of the beginning had reached the size of the palm. About this time a similar eruption appeared on the anterior surface of the chest, also spreading slowly. In three months the condition had become rather widespread, involving the greater part of the back, chest and abdomen.

* Studies, observations and reports from the dermatological department of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

the scalp being also affected at this time. Simultaneously with the appearance of the condition on the scalp the child became extremely fretful during the act of defecation, at times refusing to have a stool. On examination the anus was found to be involved in the general eruption.

The child had been treated by various local remedies but had received no medical attention for some weeks previous to admission into the hospital.

Physical Examination.—On examination the child was found to be much undernourished, weighing only 21 pounds. The scalp was covered with a scant growth of fine blond hair. Over the occiput and symmetrically over both temporal regions were many discrete, follicular, pinhead sized papular lesions of a yellowish brown color, the majority of which were covered with a dirty brown to black greasy scale. These scales were particularly in evidence over the occiput. On removal of the scale it was seen to consist of a thick horny plug which extended into the follicle, the papule being left with a minute funnel shaped depression in the center. Though discrete, the individual papules were



Fig. 1.—Distribution of greasy scale lesions over scalp.

rather closely aggregated, the scale formation over several of the papules giving the eruption a confluent appearance (Fig. 1). A similar condition existed over the entire back and anterior chest, extending downward onto the abdomen and the lumbar region (Figs. 2 and 3). The lesions over the back and abdomen stood out as more characteristic papules than did those of the scalp. In the axillae and inguinal regions were a number of lesions which had become ulcerated as the result of moisture and friction. The perineum, arms, hands, legs and feet were at this time entirely free from any evidence of the disease. The pruritus at times was intense, preventing the child from sleeping. The resultant scratching produced many excoriations with crust formation and secondary staphylococcic dermatitis.

The eyes presented nothing abnormal. The mucous membranes of the conjunctivae were anemic, but evidenced no lesions. The mucous membranes

of the mouth were anemic. The tongue presented a slight furring but no other manifestation of disease. The tonsils were slightly enlarged and injected. On the hard palate, 0.5 cm. within the margins of the teeth, in place of the usual furrowed or rugous condition, were a number of pink to white papular lesions, firm to pressure and the size of a wheat seed. Those posteriorly were ulcerated and covered with a gray membrane, resembling very much the moist papules of a syphilid. They were symmetric in their distribution and painful to manipulation.



Fig. 2.—Distribution of lesions over chest.

At the mucocutaneous border of the anus was a distinct circular formation of papular efflorescences, each papule of an oval shape and the size of a wheat grain. They were arranged end to end, were of a yellowish red color, slightly infiltrated and very tender to the touch, causing much pain on defecation (Fig. 4). Two of the lesions had become vegetative and presented an ulcerated flat surface.

An examination of the ears made by Dr. W. E. Sauer revealed many small rather firm papules along the external auditory canal. These resembled closely small vesicles but could not be ruptured. Both membrana tympani were perforated, discharging pus freely.

An examination of the lungs and heart gave no evidence of disease. The abdominal viscera were apparently normal. The lower border of the liver was



Fig. 3.—Distribution of lesions over back.

palpable one finger's breadth below the costal margin. The spleen was not palpable nor were there lymph gland enlargements.

Laboratory Examination.—The urine was found to be normal on daily examination during the stay in the hospital. The blood picture showed a hemoglobin content of 70 per cent. and 3,800,000 red cells. There was no

variation in the size and shape of the cells. The white blood count averaged about 11,000 with a differential count as follows: polymorphonuclear neutrophils, 61 per cent.; eosinophils, 1 per cent.; large mononuclear lymphocytes, 17 per cent.; small mononuclear lymphocytes, 16 per cent.; transitionals, 5 per cent.

The Wassermann reaction and von Pirquet test were negative. Blood culture was negative. Examination by smear, culture and guinea-pig inoculation with the discharge from the ear failed to reveal the tubercle bacillus.

Histopathology.—Skin tissue showing the more characteristic types of follicular papules was excised from the scapular region and the abdomen. It was not possible to obtain specimens from the anal region. The corium showed little change under the earlier lesions taken from the scapular region where they were inaccessible to scratching; that taken from the abdomen showed a rather marked infiltration of leukocytes, due no doubt to secondary infection. There was no appreciable change in the elastic tissue. The vessels showed only slight dilatation. There was no change in the connective tissue except in the part involved in the secondary infection.

The epidermis presented many changes from the normal. The horny layer was most involved, presenting a marked hypertrophy with a parakeratosis. In



Fig. 4.—Circularly arranged excrescences at mucocutaneous border of the anus.

that portion nearest the rete were numerous cells which had retained their nuclei, the latter being larger in many instances than those of the prickle cells. These nuclei were round and enclosed within a vacuolated space, possibly the remnant of the doubly contoured cell seen in the rete. The stratum granulosum was everywhere much thickened. The characteristic cell, the so-called "corps rond," though not as pronounced as in more advanced cases, was present in all stages of formation. They were seen only around the follicular orifice. These cells consisted of rounded or polygonal shaped membranes surrounding a vacuolated space within the center of which was the inner cell membrane with its large round granular nucleus. These cells varied in size from that of the normal rete cell to twice the size and were located mainly in the upper rete and granular layers. At infrequent intervals were small clear areas in which complete cellular degeneration had occurred. The basal layer was intact except in those areas involved in secondary infection where leukocytes had invaded the rete to the horny layer. On the whole, the microscopic changes involved only the follicular orifice, the intermediate spaces being involved only superficially.

Clinical Course.—During the seven weeks' stay in the hospital the child showed slight improvement under roentgen-ray therapy. The condition about the anus was almost completely relieved. Local applications were of little benefit. The child left the hospital on the fourth day of March reporting at weekly intervals. An examination four months after our first observation showed the condition to be rapidly progressive. The scalp, chest and back showed a complete recurrence with an exaggeration of the eruption which had been partially healed. The palms and soles also showed minute pinhead sized papules. The cubital fossae, thighs and popliteae were involved. The anal condition became more prominent with vegetative growth of all the lesions and extension of the eruption onto the surrounding skin. These papules had all become ulcerated and were a constant source of distress. The mouth presented virtually the same picture as on the initial examination. The ears, though much improved, continued to show a purulent discharge. The child's weight was the same as on first admission. The patient died on May 31, about five months after being presented to us. The cause of the death could not be ascertained though the family attributes it directly to the disease of the skin. Necropsy was not obtainable.

COMMENT

Darier's disease is generally understood to be a disease of early adult life, starting usually between the ages of 8 and 20 and extending on beyond middle age. Of those cases which have been reviewed only six have been found to occur in the first five years of life. DeAmicis,¹ Mourek² and Schwab³ collected three cases having their onset in the first five years of life, Mook⁴ and Malinowsky⁵ each reporting similar cases. White⁶ reported a case beginning at 5 years, while Boeck,⁷ Bowen⁸ and Thibault⁹ have individually listed cases having their origin in the first decade. The case included in this report gave a history of onset at about the age of 18 months and was studied early in the course of the disease.

That heredity plays a rôle in the etiology of the disease seems to have been proved. Trimble,¹⁰ in 1912, reported a series of five cases occurring in one family, while Boeck saw it in a father and two sons and White in a father and daughter. One of Mook's patients gave a history of the disease in other members of the family. There is nothing in the history of the present case pointing to an hereditary factor.

1. DeAmicis: *Bibliotheca Med.* **2**:3, 1894.

2. Mourek: *Arch. f. Dermat. u. Syph.* **27**:361, 1894.

3. Schwab: *Inaug. Dissert.*, Freiburg, 1902.

4. Mook: *J. Cutan. Dis.* 1912, p. 722.

5. Malinowsky: *Monatshefte*, **43**:209, 1906.

6. White: *J. Cutan. Dis.* 1890, p. 13.

7. Boeck: *Arch. f. Dermat. u. Syph.* **23**:857, 1891.

8. Bowen: *J. Cutan. Dis.* 1896, p. 209.

9. Thibault: *Annales*, July, 1889.

10. Trimble, William B.: *Observations on Keratosis Follicularis*, *J. A. M. A.* **59**:604 (Aug. 24) 1912.

McLeod¹¹ and Omerod¹² mention the affection of the mouth and tongue but give no description of the lesions occurring there. Mook speaks of raspberry-like projections on the tongue and a peculiar condition of the hard palate. Huber¹³ reported a case with lesions identical with the skin lesions on the mucous membranes. Nowhere has specific mention been made of the presence of lesions on the mucous membrane of the anus, nor has it been possible to find a record of the lesions presenting in the auditory canal. As stated earlier, this case seems unique in its peculiar mucous membrane eruption.

Regarding treatment, there is little benefit to be derived from the means now at hand. The roentgen ray seems to offer the best chance for relief, which may be but palliative and is indeed impracticable in very early life.

11. McLeod: *Brit. J. Dermat.*, 1904, p. 322.

12. Omerod: *Brit. J. Dermat.*, 1904, p. 322.

13. Huber: *Arch. f. Dermat. u. Syph.*, 1903.

REFRACTOMETRIC STUDIES WITH THE SERUMS OF NORMAL RABBITS RECEIVING INTRAVENOUS INJECTIONS OF ARSPHENAMIN AND NEO-ARSPHENAMIN*

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PHILADELPHIA

In a previous publication¹ the following changes were observed in the serums of syphilitic patients during the course of eight intravenous injections of arspenamin (from 0.4 to 0.6 gm.) and neo-arsphenamin (0.9 gm.), each drug being given at weekly and semiweekly intervals.

1. Classified according to the Wassermann reaction of the serums before treatment, there were no sufficiently constant or striking differences to warrant differentiating between the strongly and the weakly positive series.

2. Considered according to the intervals of injection, the relative amounts of globulins showed more rapid decline during weekly arspenamin than during neo-arsphenamin injections.

During semiweekly periods of administration, the changes were about the same.

3. Classified according to the degree of resistance of the patients to antisymphilitic treatment (as indicated by repeated Wassermann tests) it was observed that when the Wassermann reaction remained persistently positive, the refractive index, the percentage of total proteins and the relative amount of globulins of the serums showed little or no tendency to drop below their original values. When the Wassermann reaction, on the other hand, became very readily negative, the curves fell with more or less regularity during the course of injections.

PLAN OF INVESTIGATION

The aim of the present investigation was to make similar studies with the serums of normal rabbits. These subjects were investigated:

1. Refractometric studies with the serums of normal rabbits.
2. The influence of intravenous injections of alkalized solutions of arspenamin.

* From the Dermatological Research Institute and the Wistar Institute of Anatomy, Philadelphia.

*Investigation aided by funds accruing from the preparation of arspenamin.

1. Tokuda, K.: Refractometric Studies in Human Syphilis, With Special Reference to Changes Occurring During Treatment With Arspenamin and Neo-Arsphenamin, *Arch. Derm & Syph.* **3**:512, 1921.

3. The influence of intravenous injections of solutions of neo-arsphenamin.

TECHNIC

Normal female rabbits (kept under constant conditions of diet, etc.) were used in these experiments. They were injected intravenously with arsphenamin (2 per cent. alkaline, disodium solution) or with neo-arsphenamin (4 per cent. aqueous [neutral] solution) in various doses per kilogram of body weight, at intervals of seven days as outlined in the accompanying protocols. Specimens of blood, varying in amounts from 5 to 10 c. c. were obtained from one ear vein, and the injection was made in the other. No xylene was used to rub the ear, in order not to vitiate the refractometric readings. The blood was received in sterile test tubes, and was centrifugalized to obtain clear serum. The refractive index and percentage of proteins of the serums were determined by Robertson's microrefractometric method.²

REFRACTOMETRIC STUDIES WITH NORMAL RABBIT SERUMS

In Table 1, I have summarized the results of observations on normal rabbits before treatments. The refractive index in this series of rabbits (whose weights varied between 2,160 and 2,550 gm., their average weight being 2,329 gm.) ranges between 1.34720 and 1.34976, the average being 1.34837. The percentage of total proteins varies between 5.17 and 6.08 per cent., the average value being 5.54 per cent. The percentage of albumin varies between 4.01 and 5.12 per cent., the average being 4.47 per cent.; the percentage of globulin varies between 0.50 and 1.70 per cent., with an average of 1.08 per cent.; the globulin varies between 10 and 29 per cent. of the total proteins, the average being 19 per cent.

These values of the refractive index are slightly lower than those obtained by Hatai³ on normal rats, ranging in age from 92 to 597 days.

The values of the refractive index of the serum, total proteins, total globulin, and relative amounts of globulin are lower than those obtained by Toyama⁴ on normal rats, ranging in age from 94 to 385 days, except that the total albumin and the relative amount of albumin are higher.

2. Robertson, T. B.: A Microrefractometric Method of Determining the Percentage of Globulin and Albumin in Very Small Quantities of Blood Serum, *J. Biol. Chem.* **22**:233-239, 1915.

3. Hatai, S.: The Refractive Index of the Blood Serum of the Albino Rat at Different Ages, *J. Biol. Chem.* **35**:527-552 (Sept.) 1918.

4. Toyama, I.: Relative Abundance of Serum Proteins in Albino Rats at Different Ages, *J. Biol. Chem.* **38**:161-166 (May) 1919.

Righetti⁵ has obtained similar results on normal rabbits. Comparing our results on normal rabbits with those of Wells,⁶ we observe that generally, our percentages of total proteins, albumin, and globulin are lower; our relative amounts of globulin are similar.

In comparing our figures for normal untreated rabbits with the data found in the literature on human blood, we observe that, in general, the values for the former are *lower* than those obtained either on normal or on syphilitic human blood.

TABLE 1.—SUMMARY OF REFRACTOMETRIC STUDIES ON NORMAL FEMALE RABBITS

Rabbit	Body Weight, Gm.	Refractometric Index	Percentage of			Relative Amounts of	
			Total Protein	Albumin	Globulin	Albumin	Globulin
1	2,550	1.34860	5.70	4.44	1.26	78	22
2	2,460	1.34786	5.53	4.53	1.00	82	18
3	2,035	1.34720	5.26	4.53	0.73	86	14
4	2,235	1.34794	5.32	4.01	1.31	75	25
5	2,285	1.34846	5.68	4.66	1.02	82	18
7	2,205	1.34976	6.08	5.12	0.96	84	16
8	2,160	1.34794	5.17	4.83	0.50	90	10
9	2,490	1.34820	5.23	4.02	1.21	77	23
10	2,490	1.34982	5.91	4.21	1.70	71	29
Average values	2,329	1.34837	5.54	4.47	1.08	81	19
Limits of variation							
From.....		1.34720	5.17	4.01	0.50	71	10
To.....		1.34976	6.08	5.12	1.70	90	29

REFRACTOMETRIC STUDIES WITH THE SERUMS OF NORMAL RABBITS TREATED WITH ARSPHENAMIN AND NEO-ARSPHENAMIN

(a) *The Effects of Massive Doses of Arsphenamin.*—*Experiment 1.*—Rabbit 1, weighing 2,555 gm., was injected intravenously with a 2 per cent. solution of arsphenamin, at intervals of seven days, the dose being 0.05 gm. per kilogram of body weight. This dose is ten times as great as that used in human antisyphilitic treatment. The refractometric determinations were carried out at the end of every week. The animal was slightly emaciated at the end of the first week, but gained weight thereafter.

The observations are summarized in Tables 2 and 3. The refractive index shows an initial drop with the first and second injections, then rises continuously until the sixth, and finally falls.

The curves for percentages of total proteins, albumins and globulins, and relative amounts of globulin, are similar to the last, indicating that changes in the refractive index are largely due to alterations in the serum proteins.

(b) *The Effects of Massive Doses of Neo-Arsphenamin.*—*Experiment 2.*—Rabbit 4 was injected at weekly intervals with neo-arsphenamin (in 4 per cent. solution), the dose being 0.05 gm. per kilogram of body weight.

5. Righetti, H.: An Investigation of the Ratio of Globulins to Albumins in the Blood Serum of Normal Rabbits and of Rabbits Immunized Against *Bacillus Typhosus*, Univ. of Calif. Pub. Physiol., Berkeley, **2**:205-214, 1916

6. Wells, C. E.: The Influence of Age and of Diet on the Relative Proportions of Serum Proteins in Rabbits, J. Biol. Chem. **15**:37-41, 1913.

In general the results (Tables 2 and 3) are similar to those observed in Experiment 1. This animal lost 335 gm. in weight during the first week. It was emaciated slightly throughout the treatment, but recovered and gained weight during the latter part of the experiment.

(c) *The Effects of Small (Therapeutic) Doses of Arspenamin.*—Experiment 3.—Rabbit 8 was injected with arspenamin at weekly intervals, the dose, 0.01 gm. per kilogram being comparable to that used in human antisyphilitic therapy.

The refractive index, the percentage of total proteins and albumins showed more of a tendency to downward gradations than in the previous experiment. The relative amount of globulin and total globulin was increased as a result of the treatment.

TABLE 2.—(EXPERIMENT 1, RABBIT 1.)—THE EFFECTS OF MASSIVE DOSES OF ARSPHENAMIN (0.05 GM. PER KILOGRAM), GIVEN AT WEEKLY INTERVALS

Injection	Date	Body Weight, Gm.	Amount Injection, C.c.	Refractometric Index	Percentage of			Relative Amounts of	
					Total Protein	Albumin	Globulin	Albumin	Globulin
Before injection	12 10/19	2,550	6.38	1.34863	5.70	4.44	1.26	77.9	22.1
1	12/17/19	2,455	6.14	1.34752	5.35	4.33	1.02	80.9	19.1
2	12/22/19	2,625	6.65	1.34701	4.88	3.91	0.97	80.1	19.9
3	12/29/19	2,685	6.71	1.34777	5.30	4.24	1.06	80.0	20.0
4	1/5/20	2,685	6.71	1.34820	5.63	4.27	1.36	75.8	24.2
5	1/12/20	2,600	6.50	1.35000	6.80	5.39	1.41	79.3	20.7
6	1/19/20	2,990	7.48	1.35071	6.66	5.21	1.45	78.2	21.8
7	1/26/20	2,850	7.13	1.34959	6.22	4.86	1.36	78.1	21.9
8	2/2/20	2,855	7.13	1.34829	5.56	4.43	1.13	80.0	20.0

TABLE 3.—(EXPERIMENT 2, RABBIT 4.)—THE EFFECTS OF MASSIVE DOSES OF NEO-ARSPHENAMIN (0.05 GM. PER KILOGRAM), GIVEN AT WEEKLY INTERVALS

Injection	Date	Body Weight, Gm.	Amount Injection, C.c.	Refractometric Index	Percentage of			Relative Amounts of	
					Total Protein	Albumin	Globulin	Album'n	Globulin
Before injection	12/17/19	2,235	2.80	1.34794	5.32	4.01	1.31	75.4	24.6
1	12/22/19	2,120	2.65	1.34777	5.21	3.91	1.30	75.0	25.0
2	12/29/19	2,250	2.81	1.34572	4.04	3.29	0.75	81.4	18.6
3	1/5/20	2,265	2.83	1.34701	5.00	3.68	1.32	73.6	26.4
4	1/12/20	2,300	2.90	1.35010	6.08	4.47	1.61	73.5	26.5
5	1/26/20	2,210	2.76	1.34777	5.26	4.12	1.14	78.3	21.7
6	2/2/20	2,035	2.54	1.34701	5.00	3.79	1.21	75.8	24.2
7	2/9/20	2,065	2.60	1.34666	4.99	3.82	1.17	76.6	23.4
8	2/16/20	2,240	2.80	1.34803	5.54	4.21	1.33	76.0	24.0

The observations are summarized in Tables 4 and 5.

(d) *The Effects of Small (Therapeutic) Doses of Neo-Arsphenamin.*—Experiment 4.—Rabbit 7 was injected intravenously at intervals of seven days with neo-arsphenamin, the dose (0.015 gm. per kilogram of body weight) being similar to that used in human antisyphilitic treatment.

As will be seen from Tables 4 and 5, the refractive index of the serum remains much below its original level throughout the treatment.

The total proteins and the albumins follow a somewhat similar course. The relative amount of globulin shows a fairly progressive increase, with return to original value at the end of the period of treatment. This animal was emaciated throughout the treatment.

(e) *Detailed Analysis of the Immediate Effects of the Therapeutic Doses of Arspenamin and Neo-Arsphenamin.*—Experiment 5.—In order to obtain

TABLE 4.—(EXPERIMENT 3, RABBIT 8.)—THE EFFECTS OF SMALL (THERAPEUTIC) DOSES OF ARSPHENAMIN (0.01 GM. PER KILOGRAM), GIVEN AT WEEKLY INTERVALS

Injection	Date	Body Weight, Gm.	Amount Injection, C.c.	Refractometric Index	Percentage of			Relative Amounts of	
					Total Protein	Albumin	Globulin	Albumin	Globulin
Before injection	1/26/20	2,160	1.08	1.34794	5.17	4.67	0.50	90.3	9.7
1	2/ 2/20	2,030	1.02	1.34692	4.92	4.23	0.69	86.0	14.0
2	2/ 9/20	2,080	1.04	1.34684	5.00	4.15	0.85	83.0	17.0
3	2/16/20	2,065	1.03	1.34649	4.70	3.91	0.79	83.2	16.8
4	2/24/20	1,970	0.99	1.34692	4.91	4.22	0.69	85.9	14.1
5	3/ 1/20	1,990	0.99	1.34752	5.37	4.52	0.85	84.2	15.8
6	3/15/20	2,160	1.08	1.34709	5.33	4.63	0.70	86.9	13.1
7	4/12/20	2,060	1.34709	5.01	4.32	0.69	86.2	13.8

TABLE 5.—(EXPERIMENT 4, RABBIT 7.)—THE EFFECTS OF SMALL (THERAPEUTIC) DOSES OF NEO-ARSPHENAMIN (0.015 PER KILOGRAM), GIVEN AT WEEKLY INTERVALS

Injection	Date	Body Weight, Gm.	Amount Injection, C.c.	Refractometric Index	Percentage of			Relative Amounts of	
					Total Protein	Albumin	Globulin	Albumin	Globulin
Before injection	1/12/20	2,205	0.83	1.34976	6.08	5.12	0.96	84.2	15.8
1	1/19/20	2,160	0.81	1.34898	5.82	4.78	1.04	82.1	17.9
2	1/26/20	1,945	0.73	1.34803	5.46	4.54	0.92	83.2	16.8
3	2/ 2/20	1,940	0.73	1.34632	4.73	3.99	0.74	84.4	15.6
4	2/ 9/20	1,900	0.71	1.34666	4.89	4.00	0.89	81.8	18.2
5	2/16/20	1,950	0.73	1.34615	4.60	3.68	0.92	80.0	20.0
6	2/24/20	1,720	0.65	1.34684	4.78	3.81	0.97	79.7	20.3
7	3/ 1/20	1,765	0.66	1.34743	5.24	4.10	1.14	78.2	21.8
8	3/ 8/20	1,835	0.69	1.34641	4.62	3.90	0.72	84.5	15.5

TABLE 6.—(EXPERIMENT 5, RABBIT 9.)—DETAILED ANALYSIS OF THE IMMEDIATE EFFECTS OF SMALL (THERAPEUTIC) DOSES OF ARSPHENAMIN AND NEO-ARSPHENAMIN: ARSPHENAMIN (2 PER CENT. SOLUTION) 0.01 GM. PER KILOGRAM DOSE 1.3 C.C.

Date, 1920	Body Weight, Gm.	Refractometric Index	Percentage of			Relative Amounts of	
			Total Protein	Albumin	Globulin	Albumin	Globulin
Sept. 27	2,490	1.34932	5.91	4.21	1.70	71.2	28.8
½ hour after injection	2,490	1.34752	5.09	4.06	1.03	79.8	20.2
Sept. 28	2,490	1.34846	5.54	4.21	1.33	76.0	24.0
Sept. 29	2,350	1.34915
Sept. 30	2,340	1.34794	4.81	3.19	1.62	66.3	33.7
Oct. 2	2,340	1.34735	4.25	3.16	1.09	74.4	25.6
Oct. 4	2,360	1.34906	5.55	4.25	1.30	76.6	23.4

a more accurate knowledge of the changes which occur in the blood serum during the first few days following immediately after an injection of arspfenamin or neo-arsphenamin, two normal animals (rabbits 9 and 10) were injected intravenously with doses similar to those used in Experiment 5. The blood was examined at intervals of one-half hour, and one, two, three, five and seven days after a single injection.

Both rabbits showed a decrease in the refractive index of the serum within half an hour after injection, the change being much more marked and irregular

when arsphenamin was used. After twenty-four hours, increasing figures were observed in both animals. The subsequent changes consist in a gradual and continuous fall up to five days after injection in the case of neo-arsphenamin and a decline with marked fluctuations when arsphenamin was used. Both curves return to their original level a week after the injection.

TABLE 7.—(EXPERIMENT 6, RABBIT 10.)—NEO-ARSPHENAMIN 0.015 GM. PER KILOGRAM; DOSE 0.95 C.C.

Date, 1920	Body Weight, Gm.	Refractometric Index	Percentage of			Relative Amounts of	
			Total Protein	Albumin	Globulin	Albumin	Globulin
Sept. 27	2,525	1.34820	5.23	4.02	1.21	76.9	23.1
½ hour after injection	2,525	1.34777	5.05	3.97	1.08	78.6	21.4
Sept. 28	2,560	1.34820	5.27	4.12	1.15	78.2	21.8
Sept. 29	2,450	1.34704	5.21	3.74	1.47	71.8	28.2
Sept. 30	2,450	1.34666	4.51	3.11	1.40	69.0	31.0
Oct. 2	2,480	1.34598	4.25	3.25	1.00	76.5	23.5
Oct. 4	2,480	1.34863	5.35	3.59	1.76	67.1	32.9

The curves for total proteins, albumins and globulins, tend to be parallel to the last ones described. The relative amounts of globulin tend to fall in both animals half an hour after injection. There is a marked rise evident at the end of three days. The rabbit receiving arsphenamin showed more loss of weight than the other.

SUMMARY

While it is impossible to draw any definite conclusions on the basis of so small a series of animals, the results are rather suggestive and warrant the publication of this preliminary note.

1. When massive doses of either arsphenamin or neo-arsphenamin are administered intravenously at weekly intervals to normal female rabbits, there is a temporary decrease in the refractometric index of the serum owing to a diminution of the percentage of the various proteins. Irregular fluctuations in the curves follow with a final return to approximately their original values.

2. When therapeutic doses of either of these drugs are given, there is a tendency toward decrease of the refractive index, with an increase in the relative amount of globulins.

3. If the values are plotted at frequent intervals after a single therapeutic dose of either drug, we note a fall in the refractive index of the serum one-half hour after injection. The relative amounts of globulin show an initial fall with a tendency to rise during the first few days following the injection.

4. In general, the changes induced by arsphenamin are somewhat more striking than when neo-arsphenamin is employed, perhaps because of the greater volume of fluid injected in the former case. This problem requires further experimental study.

EXPERIMENTAL WORK ON BLOOD NITROGEN IN PSORIASIS *

ROBERT C. JAMIESON, M.D.

DETROIT

The riddle of psoriasis being still as unsolved as that of the sphinx, investigations into its mysteries are always fascinating even though they prove fruitless.

Up to 1913, a great deal of empiric experimental work had been done to discover the cause and cure of psoriasis and as many theories had been advanced as there were investigators. At that time Schamberg¹ and his associates began a systematic, scientific investigation which apparently covered the entire known field of experimental medical knowledge, having all possible methods placed at their disposal. Their investigations are thus summed up:

In some cases a positive Wassermann reaction was elicited without a syphilitic history or symptoms, but no attempt was made to explain any possible significance. However, in using scales and culture antigens, no specific complement fixation could be obtained. Vaccine treatment and inoculation experiments resulted in failure, but a diplococcus "X" was found in five cases and one blood culture, the ultra microscope showing actively motile bacillary bodies in all but two of nineteen cases. Experimental work on the question of nitrogen retention disclosed the fact that persons suffering from psoriasis are capable of retaining nitrogen to a remarkable degree, much greater than is observed in any other condition. Schamberg and his associates are "strongly inclined to believe that a high or even relatively high nitrogen diet has a baneful influence on psoriasis" and "feel that there can exist little doubt as to the favorable influence of a low nitrogen diet on the eruption of psoriasis." Their explanation of the possible *modus operandi* of this change is very interesting:

The epithelial cells of the skin keep on growing as long as there is "available" or "mobilizable" protein in the system. When this is exhausted, their growth is checked. And this, in our estimation, may account for the frequent spontaneous improvements in cases of psoriasis. By keeping the patient on a low protein diet, we hasten this point of "exhaustion." We hasten the slow starvation of the epithelial cells. By keeping the patient on a high protein diet, we stimulate the growth of the epithelial cells and thus delay improvement.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Schamberg, Kolmer, Ringer and Raiziss: *J. Cutan. Dis.* **31**:697 and 799, 1913.

OTHER INVESTIGATIONS IN THE LITERATURE

Dark-field illumination in psoriasis and in other skin diseases was carefully carried out by Ketron,² in 1914, with negative results. Formations were found in the majority of preparations taken from the skin and blood, which resembled live organisms, but it is stated that they were merely products of normal serum and red blood corpuscles. Bacteriologic methods and injection of serum and epithelial preparations were likewise negative.

In 1917 and 1918, Van Alstyne³ reported good results obtained from the continued injection of a nitrogen extract prepared from alfalfa and millet seed by Beebe's method. This was done with the idea of educating the cells to assimilate the retained nitrogen by small and increasing nitrogen injections. Several attempts were made by us to follow up this work but, in general, failure resulted. One or two patients with severe cases, however, reported the following year that their lesions had not recurred either so plentifully or persistently. This is the only improvement noted.

Cook⁴ suggests staphylococcus and streptococcus as causative factors, and reports ten cases treated with emetin hydrochlorid, these patients having psoriasis associated with pyorrhea. Five of these had the endameba present, three having pyorrhea alveolaris, two of which were free from psoriasis after the pyorrhea was cured. The condition of two patients having the endameba present remained unchanged, while four having neither pus nor endameba also showed no change. One patient with psoriasis recovered after a seminal vesiculitis was cleared up, another following cure of a rectal fistula, a third after tonsillectomy.

The frequent association with tonsillar disease or with removal of the tonsils is often noted, Winfield⁵ reporting six cases following acute inflammation of the tonsils. No specific organism was found in his cases, but he suggests that "tonsillar inflammation and high temperature disturbed the metabolic balance sufficiently to produce the skin disease in one predisposed."

This explanation may also be employed to account for the disappearance as well as the production of lesions, as we have seen psoriasis increase following tonsillectomy, as well as temporarily disappear following tonsillitis and typhoid fever. A most striking example was furnished by a physician suffering from psoriasis who had a severe attack of tonsillitis in November, 1919. He received several

2. Ketron: *J. Cutan. Dis.* **32**:216, 1914.

3. Van Alstyne: *Med. Rec.* **92**:538 (Sept. 29) 1917; *New York M. J.* **108**:326 (Aug. 24) 1918.

4. Cook: *New York M. J.* **104**:255 (Aug. 5) 1916.

5. Winfield: *J. Cutan. Dis.* **34**:441 (June) 1916.

injections of stock staphylococcus and streptococcus vaccine, with a total disappearance of lesions for several months. In June, 1920, however, the disease had fully returned, covering large areas on the trunk and extremities.

Holland⁶ also reports three cases of psoriasis cured (?) in which there was a history of tonsillitis and arthritis.

In the work of Fox,⁷ and of Trimble and Rothwell,⁸ in which favorable results are reported following the use of autoserum, certain metabolic changes could reasonably be deduced to account for the improvement and also for the fact that chrysarobin apparently had a better effect following the use of autoserum.

The use of nonspecific protein therapy by Engman and McGarry⁹ caused temporary improvement in some cases, this possibly being accounted for by metabolic changes from hyperpyrexia or leukocytosis.

The roentgenographic and clinical studies of Levy-Frankel and Jacob¹⁰ would seem to indicate that they consider tuberculous subjects a favorable field for the development of psoriasis.

Spiethoff¹¹ found an inherited tendency in 5 per cent. or 6 per cent. of patients, and is inclined to believe that anything causing internal disturbance is liable to bring on an attack of psoriasis.

In a recent examination of many young adults, Bory¹² found 80 per cent. of cases were of recent development and that only twenty-six cases out of 129 occurred before the age of 20. He believes that the evidence points to a parasitic or infectious and not a metabolic origin. Similarly, in the case reported by Ibotson,¹³ the psoriatic lesions of seventeen years' duration were removed by an attack of exfoliative dermatitis following the ingestion of oysters.

The flora of the intestinal canal also are believed to be a source of infection in chronic dermatoses by Claveaux,¹⁴ working on the theory advanced by Danysz,¹⁵ and using autovaccine derived from intestinal bacteria. No report is given to show whether relapse occurs in these

6. Holland, E. D.: The Treatment of Psoriasis with Vaccines, *J. A. M. A.* **64**:903 (March 13) 1915.

7. Fox, Howard: Autogenous Serum in the Treatment of Psoriasis, *J. A. M. A.* **63**:2190 (Dec. 19) 1914; *J. Cutan. Dis.* **33**:616 (Sept.) 1915.

8. Trimble and Rothwell: *J. Cutan. Dis.* **33**:621 (Sept.) 1915.

9. Engman, M. F., and McGarry, R. A.: The Treatment of Certain Diseases of the Skin, *J. A. M. A.* **67**:1741 (Dec. 9) 1916.

10. Levy, Frankel and Jacob: *Bull. Soc. franç. de dermat. et syph.*, 1919, No. 8, p. 324.

11. Spiethoff: *Med. Klin.* **10**:1665-1667 (Nov. 8) 1914.

12. Bory: *Progrès méd.* **35**:281 (June 26) 1920.

13. Ibotson: *Lancet* **2**:472, 1914.

14. Claveaux: *An. de Fac. de med., Montevideo*, **5**:411 (July, Aug.) 1920.

15. Danysz: *Bull. méd., Paris* **34**:155 (Feb.) 1920.

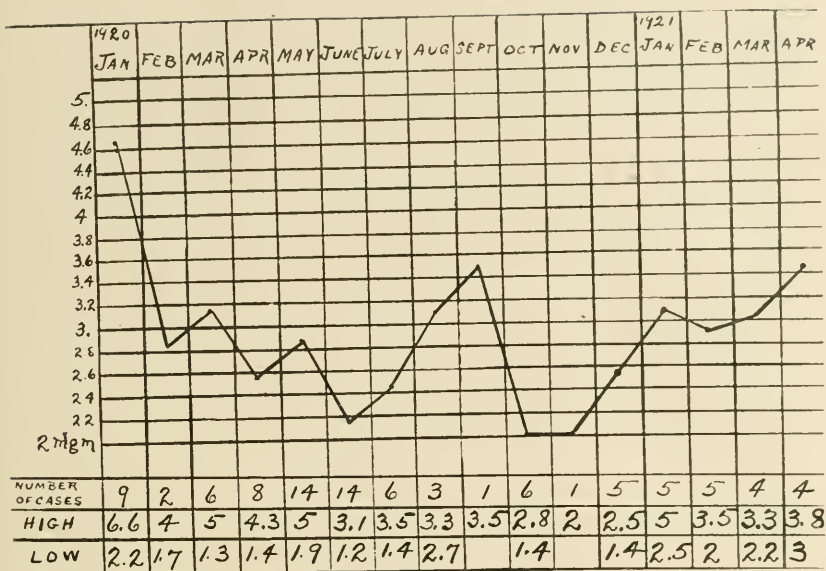


Chart 1.—Curve of average uric acid estimations.

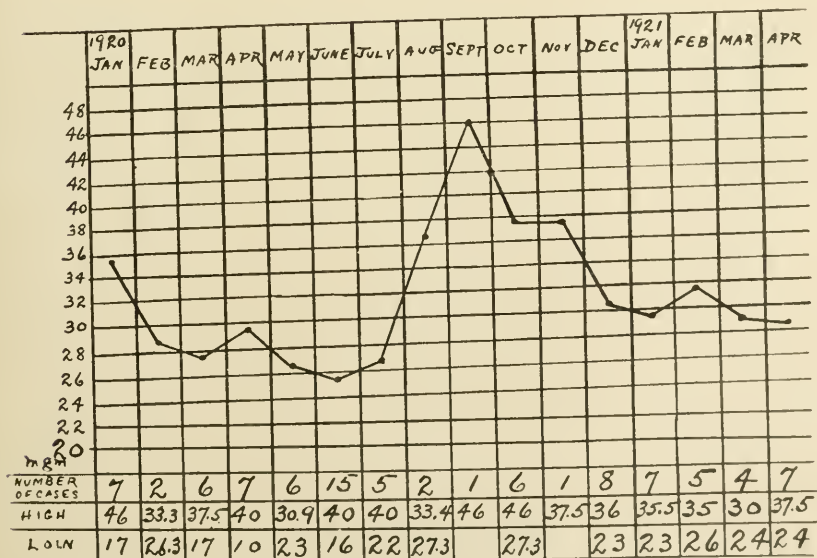


Chart 2.—Curve of average total noncoagulable nitrogen.

cases or whether the patients are cured. De Rezende¹⁶ also reports results similar to those of Engman and McGarry,⁹ who used non-specific protein therapy intravenously, with temporary benefit. De Rezende used normal horse serum and prompt improvement followed. No later reports on the "cure" are given.

All these reports would seem to indicate that psoriasis can be influenced favorably or unfavorably by certain types of metabolic disturbances of sufficient intensity, and it has seemed to us that the chemistry of the noncoagulable nitrogen of the blood might afford some clue. Sweitzer and Michelson,¹⁷ in their work on acidosis, also state their belief that patients with psoriasis should show metabolic change, but they could find no marked change in the alkali reserve. In four cases, however, in which they did a complete blood chemistry, they found an increase of urea nitrogen. Three of these cases had marked focal infection, one a marked arteriosclerosis. Removal of the foci of infection in the last case improved the general condition so much that the inveterate psoriasis yielded to treatment promptly. They recommend that persons suffering from psoriasis have a thorough examination by competent internists, especially for infected foci.

Our present understanding of the function of the renal glomeruli and tubules with regard to the excretion of nitrogenous products would seem to indicate that these products, in varying proportions, could be retained in the blood even in psoriasis, which has always been referred to as a "disease of the healthy."

AUTHOR'S INVESTIGATIONS

We determined to investigate empirically as many cases as possible over a given period of time without any attempt being made to influence the course of the disease by either internal or external medication. Realizing, also, that many cases automatically clear up partially or completely, no attempt was made to alter the patients' mode of living or diet—in other words, to make periodic examinations of the blood of these patients for one year (through all seasons), to determine, if possible, whether the nitrogenous constituents varied according to the severity of the disease or were influenced by the seasons. We also recognized the fact that the dietary regimen changes at times during the year, but all patients were treated in a similar manner. Analyses were also made in a number of normal negroes on account of the well-known rarity of the disease in that race. It was difficult at times to keep control of the dispensary patients merely for blood examina-

16. De Rezende: *Brazil-med.* **34**:425 (July 3) 1920.

17. Sweitzer, S. E., and Michelson, H. E.: *Acidosis in Skin Diseases*, *Arch. Dermat. & Syph.* **2**:61 (July) 1920.

tions, but some of them were intelligent enough to cooperate with us. Examinations were also made in a few cases of normal whites. Since January, 1921, we have also made urea estimations to determine whether our cases showed changes corresponding to those of Sweitzer and Michelson.

In following up this line of investigation, we were influenced by the firm belief in the metabolic etiology of psoriasis, especially since the work of Schamberg and his associates, and in consideration also of the following factors: first, the change in lesions according to the change in seasons in many cases, and according to change of residence, without any other therapeutic aid; second, the often noted tendency to familial psoriasis which is becoming more evident than in former years, the rarity of psoriasis in negroes, the improvement immediately following typhoid fever and similar disturbances, the exacerbations and so-called cures reported in cases of severe tonsillitis, the frequency of inception following vaccination and the incidence in infancy.

With few exceptions, the blood specimens were all drawn at approximately the same time in the morning and mixed with potassium oxalate to prevent clotting. Nitrogen determinations were made by the Folin method and were done in Buhl Laboratory of Harper Hospital. As ambulatory patients cannot be kept under constant supervision, some elements of error must necessarily creep in; however, all the work was done under the same conditions in all cases and was carried out as accurately as possible with the facilities at our disposal.

The total number of cases of psoriasis included in this investigation was forty-five, some of the patients having only a few nitrogen determinations, others returning regularly at monthly intervals. Of these cases, many were extremely extensive and severe; in others, the patients had only a small number of lesions of a rebellious type. I realize that the number of cases examined is small and that the nitrogen determinations are too few in number and have not been carried out for a period long enough to enable any definite conclusion to be drawn; but this is to be regarded merely as a preliminary report, and the work will be carried further if results are satisfactory in this and other work contemplated.

In an analysis of the uric acid determinations, an average is taken for each month during the year. Early in the work it was noted that the total noncoagulable nitrogen was almost invariably well within the normal limits of 25-35 mg. per 100 cubic centimeters of blood. At that time, however, many reports were returned showing a marked increase in uric acid content, and we determined to follow up the uric acid nitrogen only from that time (February, 1920). We were also influenced in this by a report from a physician who had taken cinchophen

for relief of some neuralgic condition and who had noted improvement of a parapsoriatic (lichenoid) patch on one elbow, this improvement being both subjective and objective.

The average uric acid estimations by months, beginning with January, 1920, are presented in Table 1.

TABLE 1.—URIC ACID ESTIMATIONS

1920	No. of Cases	Average, Mg.	High, Mg.	Low, Mg.
January	9	4.68	6.6	2.3
February	2	2.85	4.0	1.7
March	6	3.12	5.0	1.3
April	8	2.56	4.3	1.4
May	14	2.89	5.0	1.9
June	14	2.14	3.1	1.2
July	6	2.45	3.5	1.4
August	3	3.1	3.3	2.7
September	1	3.5	3.5	3.5
October	6	2.0	2.8	1.4
November	1	2.0	2.0	2.0
December	5	2.54	2.5	1.4
1921				
January	5	3.12	5.0	2.5
February	5	2.92	3.5	2.0
March	4	3.02	3.3	2.2
April	4	3.45	3.8	3.0

The average total noncoagulable nitrogen estimations beginning with January, 1920, are presented in Table 2.

As will be noted by reference to the chart, the uric acid averages for each month from January, 1920, through April, 1921, are given, the number of examinations made in each month being noted also.

TABLE 2.—NONCOAGULABLE NITROGEN ESTIMATIONS

1920	No. of Cases	Average, Mg.	High, Mg.	Low, Mg.
January	8	35.5	46.0	17.0
February	2	28.8	33.3	26.3
March	6	27.6	37.5	17.0
April	6	29.3	40.0	10.0
May	6	26.6	30.9	23.0
June	15	25.4	40.0	16.0
July	5	26.8	40.0	22.0
August	2	36.7	33.4	27.3
September	1	46.0	46.0	46.0
October	5	37.6	46.0	27.3
November	1	37.5	37.5	37.5
December	8	30.6	36.0	23.0
1921				
January	7	29.5	35.5	23.0
February	5	31.5	35.0	26.0
March	4	29.0	30.0	24.0
April	7	28.4	37.5	24.0

For January, 1920, the average was high, 4.68 mg., the averages for the succeeding months ranging from 2 mg., in October and November, to 3.5 mg., in September. The September reading is hardly fair, however, as only one examination was made that month. By comparison with the normal amount of uric acid (2-2.5 mg.) it will be seen that these averages are well within the normal limits with the exception of that for January, 1920. In the light of subsequent examinations, made principally on the same patients, we are forced to conclude that the high January average was due to an error in technic.

It will be recalled that, at least in Michigan, the winter of 1919-1920 was very much prolonged and that our patients having psoriasis did not show the usual spontaneous improvement with warm weather, as the summer was very cool and had little sunlight. Most of the cases, however, showed the most improvement in October and November and have had their relapses delayed this winter, new lesions not appearing until the winter was well advanced (February and March). It will be noted that the uric acid average is also increased at that time.

In spite of the fact that the patients showed little spontaneous improvement in the early summer, the uric acid readings were low (2.1-2.5) in June and July, coincident with the first warm weather, the season when improvement would usually be expected. The curve is also low, however, in October and November, when most of the actual improvement occurred. The number of readings in these months is not sufficient for great accuracy.

A few of the cases of most interest may be reported in greater detail.

REPORT OF CASES

CASE 1.—A man, white, aged 26, with good general health, had at 16 begun to develop lesions. He later was covered with large lesions, every part of the body, including the scalp, being thickly crusted. In 1916-1917 he became almost free by the use of the roentgen ray, mercury vapor arc light, chrysarobin and sunlight. While in the army he remained quite free, but since discharge he had had a partial recurrence, on the arms and body only. He is taking no treatment at present, and the lesions are remaining unchanged. His diet is his usual mixed one and has been the same for several years. The uric acid readings, in April, August and December, show slight variations (0.6 mg.), being highest (3.1) in August. There is, however, no coincident change in lesional characteristics. The total nitrogen content is within normal limits.

CASE 2.—A boy, white, aged 10 years, with general health good, and of Polish descent, had had a generalized psoriasis of severe type for two or three years, which covered his arms, legs, body and scalp with large patches overlaid by mortar-like crusts. Great improvement followed the use of the usual remedies and the ultraviolet ray, so that in January, 1920, the lesions were few and scattered. The uric acid readings were only twice above normal,

being 3.5 mg. in September, 1920, and 3.2 mg. in April, 1921. These occasions did not correspond with any variations in lesions. The average reading was 2.43 mg. of uric acid per hundred c.c. of blood.

CASE 3.—A man, white, aged 25, a butcher by occupation and perfectly healthy, had been covered with large plaques from head to foot for twelve years, the scalp being thickly involved with mortar-like crusts. The usual external and internal treatment would successfully remove the lesions temporarily, but they constantly recurred. The recurrence had never been so severe since the use of the roentgen ray and sunlight, nor since using injections of alfalfa extract according to Van Alstyne's method. While in perfect health, the patient's occupation gave him the opportunity of eating largely of raw meat, often 2 or 3 pounds daily, and his uric acid reading (3.1) was made in June while extensively covered with lesions. Unfortunately, only one blood nitrogen estimation could be made, but that is of interest as being the only one made in June that was at all high, the others ranging from 1.6 mg. to 2.6 mg. His ameliorated condition may now be due to his reduced protein intake. For the past six months, to January, 1921, his body and scalp have been almost entirely free. A recent relapse has nearly covered his arms and body and the last uric acid estimation showed 3.8 mg.

CASE 4.—A man, white, aged 20, had had small lesions, scattered, but covering widely separated areas for the past twelve years. This patient differed from the ordinary in that his annual improvement occurred during the winter, and he became worse in hot weather. In 1920, he was extensively covered from head to foot, and he was hospitalized in March, 1921. His lesions had apparently increased following a strong chrysarobin ointment. On his normal diet, he had a uric acid estimation of 2.6 mg., total noncoagulable nitrogen of 35 mg. No internal medication was given, but he was placed on an extremely low nitrogen diet and at the end of three weeks his estimations were 2.2 mg. uric acid, 28 total nitrogen. Two weeks later, however, following his return to normal diet his uric acid estimation had risen to 3 mg., the total noncoagulable nitrogen remaining 27 mg. At the time of the last estimation, the lesions were almost gone, after alpine sun and roentgen-ray treatment.

CASE 5.—A woman, white, aged 24, had had a very extensive and extremely rebellious case, refractory to all treatment. She apparently improved for a time under chrysarobin and ultraviolet light treatment. At this time she married and became pregnant about November, 1919. Her lesions were even more refractory during pregnancy than before, but uric acid estimations were almost always low, except in March (3.3 mg.), ranging from 1.4 mg. to 1.9 mg., but increasing in December and January, after confinement (in August), to 2.5 mg. and 2.8 mg. No estimations have been made since January, 1921.

CASE 6.—A youth, aged 17, nonpsoriatic, presented a symmetrical maculopapular eruption, involving the body, arms and legs. The lesions were mostly uniform in size, about the size of a pea; they were deep red in color; discrete in some areas, and confluent in others. The appearance was fairly abrupt and was accompanied by some pruritus. A previous attack had occurred, which gradually disappeared in the course of a few months. The Wassermann reaction was negative. There was no evidence of any illness, and the only abnormality was an excessive protein diet. Uric acid and total noncoagulable nitrogen determinations showed, respectively, 3.8 mg. and 31.5 mg. On restriction of the protein intake and regulation of the alimentary tract, improvement promptly followed.

CASE 7.—A physician, aged 45, was very extensively covered with large plaques which had received all kinds of treatment and resisted the roentgen ray. This case might be added to the cured (!) of psoriasis following tonsillitis and vaccine, as in November, 1919, he had an attack of tonsillitis and received one injection of stock vaccine. This was followed by complete disappearance of the lesions for three months. In May, 1920, the lesions had returned as extensively as ever. The uric acid estimation at that time was 5 mg., dropping to 2.6 mg. in June, the total nitrogen being 30.9 and 24 mg., respectively. This change in the uric acid content was not accompanied by any corresponding change in the lesions. The patient discontinued treatment at that time, but he has since reported that he has just completed a two weeks' treatment with chrysarobin, with satisfactory results.

CASE 8.—A woman, white, aged 29, had the first attack of psoriasis followed scarlatina, a number of years ago, after which the lesions disappeared until 1920. The lesions were of mild type, few in number and widely distributed. They have gradually disappeared in the past six months, but in inverse ratio to the uric acid estimations which gradually increased from 1.4 mg. in October, to 3.1 mg. in March. The total nitrogen content varies within normal limits.

CASE 9.—A man, white, aged 26, apparently healthy, had lesions which first appeared at the age of 7, and had always been extensive. The disease followed the usual course, frequently disappearing spontaneously during the summer months. During the past year, however, the lesions have not shown the usual improvement, and his uric acid readings were 5 mg. in March, 1920, 2.4 mg. in May, 2.5 mg. in January, 1921, 3.5 mg. in February, and 3.8 mg. in April, showing a decided tendency to increase in the late winter and early spring when his lesions were usually the worst. A great temporary improvement was noted, however, in December and January, following the experimental internal use of a recently exploited preparation, but this improvement did not continue, although the lesions have not relapsed to their former inveterate state.

CASE 10.—A normal negro, aged 28, had uric acid estimations of 3.8 mg., much higher than the average white person having psoriasis; but there was no evident cause for the increase.

CASE 11.—A normal negro, aged 26, had a normal uric acid estimation of 2.5 mg.

CASE 12.—A man, white, aged 50, had a patch of lichen planus hypertrophicus on one leg. He was otherwise normal. The uric acid and total noncoagulable nitrogen determinations were normal.

COMMENT

In comparing the uric acid curve with the total noncoagulable nitrogen curve, it will be noted that the readings vary from 25.4 mg. per 100 cubic centimeters of blood to 46 mg., and that the total nitrogen is at the low point in May, June and July; the September and October and November readings, however, being at the high point of the curve (46-37.5) which is just the opposite of the uric acid curve.

The patients examined were, with few exceptions, in apparently normal health, one was pregnant, five were nonpsoriatic controls (two

normal negroes, one lichen planus hypertrophicus, two parapsoriasis); but while the total nitrogen and uric acid readings varied in all types of cases there was no uniformity in the variation. Likewise, it could not be said that there was any apparent uniformity in the manner of the low or high point in either curve coinciding with improvement or increase in psoriatic lesions.

Since the work of Schamberg and his associates in showing the retention of nitrogen even on low protein intake, we have been convinced that psoriasis is a disease in which metabolic disturbances are at fault. When the many different reports on psoriasis from all parts of the world are compared it becomes strikingly evident that many cases of true psoriasis have their origin in greatly varying preceding conditions, all of which, however, are conditions which may produce a profound disturbance in the body metabolism. These disturbances are also capable of producing remissions of the psoriasis, as well as being the genesis, and it would thus appear that psoriasis is a definite clinical dermatologic manifestation, due to faulty metabolism induced by many underlying conditions and manifesting itself in an incomplete keratinization of the dermal cells.

If, then, further investigation shows that the retained nitrogen is not in the blood, is there any portion of the body except the cells where it could be stored? Schamberg¹ states that a low protein diet retards cell growth, while a high protein diet stimulates it, by supplying more available nitrogen. Improvement following sunlight, roentgen-ray and ultraviolet light could possibly be explained on somewhat the same theory that the action of light would either render the cells unable to take up so much nitrogen or would make the cell nitrogen more easily separable.

As the action of chrysarobin (stated by Schamberg¹⁸) is due to a firm union of the drug with the epithelial cell protein and abstraction of oxygen and might restrain the abnormal proliferative activity of the epidermal cells, the great problem in psoriasis would appear to be to keep the cell nitrogen at the lowest point, either by decreasing available protein or by enabling the cell to throw off nitrogen easily and become normally keratinized.

CONCLUSIONS

From results obtained by sixteen months' study of the blood of persons having psoriasis with regard to the uric acid and total non-coagulable nitrogen, we are unable to state that the increase or decrease of lesions corresponds with an increase or decrease of either total non-coagulable nitrogen or uric acid. From the plotted uric acid curve, it

18. Schamberg, J. F.; Ringer, A. I.; Raiziss, G. W., and Kolmer, J. A.: Summary of Research Studies in Psoriasis, *J. A. M. A.* **63**:729 (Aug. 29) 1914.

appears that it is at its low point during the warm months of summer and early fall. The total noncoagulable nitrogen curve is also similar in this respect. In a few isolated instances, however, apparently there was an increase of blood uric acid coincident with increase of lesions, but there is nothing to show that either was affected by the other.

Of eleven estimations of urea nitrogen, there were only three which showed an increase, 26 mg., 24 mg., and 18.7 mg., all being in mild cases of psoriasis. The average of the total was 14.74 mg. urea nitrogen.

THE TREATMENT OF PSORIASIS *

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During the past two years, I have been employing a method in the treatment of psoriasis which is not entirely original, but which has proved so efficient that I feel that it is worthy of wider trial, and for that reason I wish to bring it to the attention of the members of this organization. Primarily formulated as a war measure, for the purpose of getting rid of the cutaneous eruption as quickly as possible in candidates for the aviation corps, the method proved so satisfactory that we have since been employing it as a routine measure.

At the beginning, I wish to say that the procedure is one to be used only in combating the disease in the quiescent stage and not during the acute or eruptive periods. Every patient should receive a careful general physical examination before treatment is instituted, and any discoverable coexisting focal infection should be eradicated. The presence of a nephritis or of a serious heart lesion would necessarily preclude the adoption of so intensive a method of medication.

In a series of forty-two cases, the results have uniformly been good, and no untoward results have developed.

Briefly, dependence is placed on injection of a foreign protein (in the form of an autogenous colon vaccine) and the liberal use of a chrysarobin ointment, much stronger than that commonly employed (20 per cent.).

Following the discontinuance of the chrysarobin medication, arsenic, in moderate dosage, is given, to aid in preventing relapses.

In the treatment of lesions of the scalp and face, ammoniated mercurial ointment, 5 per cent., in petrolatum, or, if the scalp is very greasy, in equal parts of petrolatum and soft soap, is used.

Injections of foreign protein, and especially of blood serum (human and animal), have been employed in the treatment of psoriasis and other chronic cutaneous disorders for many years, but, so far as I know, recourse has never been had to colon vaccine for this purpose.¹

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Jamieson, Robert C.: *Trans. Am. Dermat. Assn.*, 1921, in his paper on "Experimental Work on Psoriasis," referred to the use of colon vaccine in the treatment of the disease, by Claveux, in 1919, and Danysz, in 1920. I have seen neither of these reports, but it is probable that the work of one, or both, of these investigators antedates my own.

The remedy was first suggested to me by Dr. W. W. Duke of Kansas City. His explanation of the probable benefits to be derived is set forth in the following informal communication:

We have been using a nonspecific therapy in the treatment of anaphylaxis and have observed some very good results in cases of asthma.

We thought we could perhaps get a better reaction by injecting a protein to which the patient was already sensitized than by using typhoid bacilli and similar preparations. We believed that the patient would probably be more sensitive to his own colon flora because of the fact that it had been with him for a long time, and the area of mucous membrane involved was of course very extensive. For this reason, we conceived the idea of making an autogenous vaccine from the stool, giving the first subcutaneously and in case it did not give a brisk reaction, giving it intravenously.

We almost invariably would get a brisk reaction, and it has appeared to give better results, clinically, in the treatment of anaphylactic cases than typhoid bacterin and other foreign proteins.

The vaccine is prepared by making a streak culture from the stool upon an agar slant, incubating from twelve to twenty-four hours, and then picking out the various colonies, and transplanting them on agar slants. Of course, *Bacillus coli* usually predominates, but in almost every case staphylococci of various kinds also are found. We do not make any desperate effort to identify these organisms except in the above fashion.

The dose is gauged only approximately. We make a suspension having a certain turbidity which we know by experience would amount to about one thousand million organisms per cubic centimeter. We start by giving 1-10 c.c. subcutaneously, increasing the dose 20 per cent. at each inoculation. If a reaction is not obtained after the second or third dose, we divide the amount of the last dose by ten, and give this amount intravenously. This invariably gives rise to a good reaction, sometimes causing a rise in temperature to 103° or 104°. The dose should be repeated every two to five days, depending upon the time required for the previous reaction to subside.

As to the results, I would say that we have secured better effects with autogenous colon vaccine than with any other form of foreign protein.

For several years, I have been gradually discarding the more complicated formulas in the local treatment of psoriasis and depending more and more on chrysarobin. In studying the earlier literature on chrysarobin medication, I found that the pioneers prescribed it in much stronger mixtures than those commonly employed at present. By careful clinical experimentation, we found that a 20 per cent. mixture of chrysophanic acid and petrolatum could safely be applied to one-third, or even more, of the entire cutaneous surface without giving rise to any serious local or constitutional disturbance.

The ointment is applied to the patches twice daily by means of a stiff tooth brush. The patients are, of course, kept in bed, and as a rule I have them wear a full length suit of union underwear all of the time. The eyes are bandaged at night.

The average period of confinement is seven days. Following this, any few remaining patches can be treated and kept covered (to prevent staining of the clothing), the vaccine is discontinued, and arsenic medication begun.

Only an experienced dermatologist can appreciate the utter uselessness of half-hearted treatment in an extensive case of psoriasis. For this reason, if no other, I am asking you to give this plan of treatment a thorough trial, and I shall ask you to suspend judgment on its value until you have done so.

THE PROBLEM OF PSORIASIS*

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If wisdom be necessary to the solution of a problem, I am qualified for the task in psoriasis—but on the Socratic assumption that the summation of all wisdom is to know nothing at all; and yet, I presume to claim your attention because of the ancient peradventure concerning the mouths of babes and sucklings and because of the scientific axiom that progress begins with the establishment of how little we know.

That psoriasis is a problem none will question; excluding acne, which is as much a physiologic as a pathologic process, psoriasis is the most prevalent of dermatoses—at least it is so in western Massachusetts; and this, not because of its long duration, nor its tendency to recur, but in the sense of its individual incidence.

In the universality of its occurrence, as well as in the area of involvement and the multiformity of its lesions, it is unrivaled. It is found in all countries, at all ages, in both sexes, in every class and clime and time, in the most divergent of social scales—whatever the food, the habits, the occupation or the environment of the individual. In the almanac of dermatoses it is of ancient pedigree: the zarath of the Bible, rendering its victims unfit to enter the Temple, and, hence, inviting the appellation “unclean,” this zarath, or Hebrew scale, translated very properly by an old Greek into lepron, or Greek scale, was responsible for much of the unreasoning dread aroused in the religious ages by the miscalled leprosy, which never scales. But pedigree walks with the commonplace today, when psoriasis is so widespread as to be recognizable by the tyro everywhere.

The disease may persist, unchanged, for years, or be bewildering in the rapidity of its variations, disappearing in one place to reappear in another, or it may suddenly take unto itself wings and vanish as by magic, a fortuitous circumstance that has led to many a fancied cure, with subsequent disillusionment. It affects the whole body surface, even the demimucous of the lips and genitals, but never mucous membrane proper; psoriasis here is something else. Psoriasis of the nails, an established entity, may exist as the ailment’s sole manifestation.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

POSSIBLE ETIOLOGIC FACTORS

The understanding of any phenomenon demands a knowledge of its causation, and the essential agent in psoriasis is undetermined—its very nature obscure. From the point of view of its pathologic anatomy it shares the indefiniteness of most skin affections; for the leukocyte agglomeration and hyperkeratosis mean nothing more than the obvious inflammatory process. Every cause that has ever been advanced for any disease has served time as the culprit in the commission of psoriasis; all the varied etiologic cults have here had their reign. Focal infections, gastropstosis, intestinal flora, protein sensitizations, food and drink, fish, flesh and fowl, and the refuge of every ignorance, heredity, have all been incriminated; and all with equal want of warrant except that they chanced to coincide. I know a victim, a physician, who contends that he can recover completely by abstaining from meat—but he will not. I know several who maintain that their miseries have been aggravated by meatlessness. I have a patient who asserts he never had a symptom except after an alcoholic debauch; and many patients have never indulged in the baneful beverage. One patient is a woman whose lesions begin to fade immediately with pregnancy, to disappear completely before parturition, and reappear as promptly after: a therapeutic suggestion that would limit the outlook for cures. Though these coincidences may be worth noting, as suggesting conditions without which the cause of the disease cannot flourish, psoriasis has occurred so independently of general states that it has been called the healthy man's disease—a novel conception of the principle of predisposition. There is no evidence that the disease is more prevalent among the children of those having psoriasis than among the children of those who are free from it, the belief therein being born of the readiness to notice the one and overlook the other. The notion of a cutaneous reaction to any irritant, a reaction peculiar to the affected individual, collides with the observation that curative agents are often chemical and mechanical irritants. Traumatism, often accused, has never been convicted. The frequency of psoriasis on the elbows and knees is no more a consequence of injury to these projecting angles than is its more constant occurrence on the head the result of injury to that rounded terminal. The sacrifice of serviceable teeth, with possible apical abscesses, probably long since sterile but walled-off though virulent, to the deity psoriasis is a sacrifice demanded by many another medical Moloch; and the belief in a nervous etiology dies slowly, in spite of the fact that "nerves" occur impartially in the afflicted and the exempt.

The contention is plausible, even convincing, that no internal infection could be responsible for a skin affection so extensive, so tenacious, so recurrent, without its ever affecting any other organ, and

with no repercussive influence on the general health. The argument of symmetrical manifestation, sometimes adduced in favor of a systemic infection is negligible; all diseases have a certain tendency to symmetrical involvement, and for various reasons. What, for instance, could be more striking in the symmetry of its distribution than ordinary scabies, considered, by the way, until the middle of the nineteenth century as a diathesis? The predilection of psoriasis for certain regions is of no more import than the preference of *pediculi capitis* for the head and of other *pediculi* for other sites.

CONCLUSION

Without trying to anticipate every objection to my already evident conclusion, I hasten to state it: This complex dermatosis, found everywhere, recognized everywhere, treated everywhere and intractable everywhere is only a cutaneous inflammation caused by an external organism; that, in its treatment, internal medication is pointless and profitless; that the problem of its cure, which is, after all, the only phase of the question that justifies our interest in its other phases, will be solved by concentrating our efforts on discovering this external organism, and, pending that, on trying to find, empirically, the local application most antagonistic to the growth of the unknown factor. This is not synonymous with the strongest bactericide; nor must it be an external remedy whose use may be preferred before the toleration of the disease. A patient whose vexations are principally cosmetic will not welcome being greased or discolored, or made redolent.

And to sum up with what one man through experience has found convenient of application, tolerable, inoffensive and effective: I now treat, often cure, and always help psoriasis by the use of an alcoholic lotion containing from 5 to 15 per cent., each, lactic acid, acetic acid, salicylic acid and liquor formaldehydi, with a weak percentage of mercuric chlorid. Which of these affects, directly, the agent of the disease, and which may but modify the conditions favoring its propagation the reader can only surmise—though he may lean to the latter.

A cure attained does not insure against return; no cure does. Probably no cure ever will.

OBSERVATIONS ON A NEW METHOD OF ROENTGEN-RAY THERAPY IN PSORIASIS *

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AND

H. R. FOERSTER, M.D.

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In a recent publication by Walter Brock¹ from the University Dermatologic Clinic at Kiel, the treatment of psoriasis by means of roentgen rays directed to the thymus is advocated. The good results claimed as having been obtained by this new procedure appear to warrant an inquiry by others, even if an explanation of its action as advanced by Brock is not accepted as other than speculative.

The method originated with an observation by Brock that a child with psoriasis affecting especially the head and chest, while under treatment with roentgen rays for a local effect, developed an extensive and severe outbreak, which was at the time attributed to injurious irradiation of the thyroid. Klingmueller later observed a directly contrary effect in that the disorder seemed to disappear more rapidly in adults when lesions on the neck and upper chest were included in the area exposed to roentgen rays.

These opposing results led to an investigation of the response to roentgen rays by the thyroid, parathyroid and thymus glands, singly and in combination, of the bone-marrow of the femur, and of large areas of skin, to dosages of roentgen rays varying as to amount, quality and time interval, in both young and older patients with psoriasis. It was observed that exposure of bone-marrow and of large areas of skin to roentgen rays did not influence the course of the disorder, and that irradiation of the thyroid and parathyroid glands alone was also without effect. When the region topographically related to the thymus was included in the irradiated area, the skin lesions at a distance showed improvement or grew worse. The variation in response appeared to depend on an accurate limitation of the field of entry for the rays to the thymus region and on the dose of rays administered. Attention to these factors in subsequent trials produced results which led Brock to formulate the conclusion that irradiation of the thymus, with careful attention to its surface topography, leads to disappearance of the lesions of psoriasis in from one-half to two and one-half months.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Brock, Walter: *Strahlentherap.* **11**:2 (Sept. 15) 1920.

without reference to the season of the year, with half epilation doses in adults, with 2 or 4 mm. aluminum filter, at a focus-skin distance of 20 cm., and in children over 4 years of age with one quarter to one third epilation doses, or slightly larger, with 2 or 3 mm. aluminum filter. Larger doses are followed by aggravation of the disease picture, from which it is concluded that the action is one of stimulation, for paralysis of the gland results in extension of the developing disorder. This is produced by an excessive primary dose or too early application of a further small dose with resulting cumulative action. It was determined that the second therapeutic dose is best given after an interval of two months. When dosage is properly adjusted to the age and build of the individual, complete involution of all lesions follows within from two to ten weeks, with the exception of inveterate plaques, usually at the elbows and knees. Recurrence develops from such remaining patches, which require additional local treatment for their removal.

Brock observed that an overdose, considered as first stimulating and then exhausting or paralyzing the thymus, is followed by an active development of the disorder, and that, after an interval of from three to six months, spontaneous disappearance of the lesions may occur, which he attributes to gradual regeneration of the gland with later overproduction of its secretion. Entire absence of response to the treatment was seldom noted, and a second dose always improved or aggravated the clinical picture.

Brock determined that the appropriate dosage for adults—all persons past puberty—is 10 X, 4 mm. aluminum filter, 6 on the Benoist-Walter scale, focus-skin distance 20 cm.; for slender persons 8 X, with 4 mm. aluminum filter or less; for the very robust, large boned persons 10 X with 4 mm. aluminum, or 16 X with 3 mm. aluminum. For children over 4 years $\frac{1}{4}$ to $\frac{1}{3}$ epilation dose with 2 or 3 mm. aluminum filter is considered sufficient.

The portal of entry advocated by Brock, after considerable experimentation, is bounded above by the lower border of the larynx and upper border of the clavicle; at the sides by the parasternal lines, and below by the fifth intercostal space.

Brock presents the detailed records of his cases in two groups. The first comprises eighteen cases receiving roentgen-ray treatment directed to the thyroid, parathyroid or thymus glands, singly and in combination, with varying dosage, and represents the attempts to establish a successful technic. It was observed that mixed gland irradiation directed to the jugulum with exposure of the upper sternal area was almost always effective if one-half epilation dose was given at proper intervals. Exposure of one thyroid lobe produced no response, but if struma was present a response was at times obtained, which Brock

explains by an inability to exclude the upper pole of the thymus from the field of entry for the rays.

No response followed exposure through the sternum alone, mistakenly looked on as the proper thymus area, when the jugulum and parasternal regions were not included. Large doses in adults, that is, epilation doses of 20 X, 4 mm. aluminum filter, B. W. 6, were followed regularly (seven cases) by aggravation of the lesions and gave no response in one case, while one-half or less of an epilation dose proved successful (nine cases).

Experience gained from an analysis of results in the first group led to the selection of a definite field of entry for the rays as described in the foregoing, and of a more or less standard dosage, in a second group of twenty-two cases. Four complete failures are recorded, due partly to overdosage; four gave only a partial response with early recurrence, and fourteen were successful. The failures are ascribed to a too early repetition of the treatment in two cases, and to overdosage in two young women of juvenile habitus. In the successful cases, which included types of the disorder varying from recent and mild to most extensive, infiltrated and inveterate forms, a favorable response was at times observed within fourteen days, and the lesions had involuted after from six to ten weeks. At the time of Brock's publication some of the patients had remained free from lesions for periods varying from five, six, seven, eight, ten and twelve months after the last, and at times only, treatment. Eight additional successful results are mentioned, all in persons of middle age, treated with a filtration of 3 or 2 mm. aluminum and one-half epilation dose, 8 and 6 X, respectively.

As an explanation for the action of this method of treatment Brock asserts that psoriasis is associated with hypofunction of the thymus, which can temporarily be overcome by stimulation with roentgen rays. This presupposes the existence of functioning thymus tissue at all ages and the possibility of influencing it by means of roentgen rays.

The thymus in man reaches its greatest development at the end of the second year of life, and then gradually decreases in size to a mere remnant. It may, however, continue to persist, or redevelop in certain diseases, as in exophthalmic goiter and Addison's disease. Its structure is unique among the lymphoid organs in that the lymphocytes of both cortex and medulla are supported by a reticulum of branching stellate cells of epithelial origin. By coalescence of these cells Hassall corpuscles are formed, and, according to Hart,^{1a} continue to be "formed so long as the thymus reticulum continues to exist. In this sense, then, the Hassall corpuscles are an index to the functional activity of the thymus. Hart is careful to state that he does not regard the Hassall corpuscles

1a. Hart, C., quoted by Park, E. A.: *Am. J. Dis. Child.* **12**:500 (Nov.) 1916.

as the secretory element or representing the secretory mechanism of the thymus, as some writers on this subject have done. He regards the epithelium of the thymus (the so-called reticular cells) as the true secretory element and the Hassall corpuscles merely as the index to the amount of epithelium present. 'In a word, it is possible to estimate the functioning energy of the thymus by the kind and number of the Hassall corpuscles . . . and so draw conclusions in regard to the condition of the organ at the time of death.' The formation of Hassall corpuscles is most active in childhood, and in pathologic conditions in which the thymus function is increased."

Brock points out that the histologic demonstration by Hammer and Hart of active function of the thymus even in old age—mitotic increase of lymphocytes, new formation of Hassall corpuscles, reaction to nutritional disorders—removes any doubt as to the applicability of treatment to older persons.

The thymus is known to be extremely radiosensitive, owing to the large amount of lymphoid tissue in its structure, and undergoes rapid regression, followed by rapid regeneration after roentgen-ray doses of moderate size. The changes which follow irradiation have been studied by a number of observers, and it is considered significant by Brock that enlargement of Hassall corpuscles is a constant finding. He thinks that the therapeutic effect in psoriasis is perhaps to be sought in the Hassall corpuscles, a cell type which predominates in the thymic remnant of adults, from which lymphoid elements have almost disappeared. He draws the conclusion that with increasing age of the patient and decrease in size of the thymus remnant, with consequent decrease in radiosensitiveness, the total dose must be increased in order to secure a favorable response, and he claims that his results are proof of this.

In support of his belief that psoriasis is associated with hypofunction of the thymus, Brock cites the rarity of the disease in early childhood when the thymus is at the height of its activity; its non-occurrence in status thymolympathicus and in true thymus hyperplasia; the aggravation of the disease during pregnancy and lactation when the thymus undergoes involution and presumably decrease in function; and the frequent development of psoriasis during puberty, when involution of the thymus occurs.

The theory recently advanced by Samberger of Prague that psoriasis is a parakeratotic diathesis reacting to external irritants with a defect in keratinization finds a supporter in Brock. He believes he has found the factor which secondarily produces psoriasis and constitutes the foundation for the parakeratotic diathesis in a lack of thymus secretion, which converts abnormal into normal keratinization, even though only temporarily.

Samberger claims that the parakeratotic diathesis is a dyscrasia of the epithelial cells destined for keratinization, and Brock believes these can be influenced toward a normal process of keratinization by means of stimulating doses of roentgen rays applied to the thymus.

Heretofore irradiation of glandular structures has been done to secure a destructive effect and for the purpose of diminishing secretion in organs in a state of hyperactivity. Stimulation of glandular structures in a condition of hypofunction is a new procedure. Stephan² has irradiated the spleen in a severe purpura in a patient with cervical tuberculous adenitis, and observed a marked though transitory effect on the coagulation time. Several others have undertaken researches on organ stimulation (kidney, pancreas, spleen) in problems connected with internal medicine, and in a recent contribution Petersen and Saelhof,³ of the University of Illinois, state "that it is probable that the indications of roentgen-ray therapy in the treatment of internal diseases will find marked extension if proper recognition is given the possibility of organ stimulation by such physical means."

This statement applies with equal force to dermatology. A subject of such importance to dermatology as the treatment of psoriasis, approached by a new method as advocated by Brock, appeared to us to warrant further inquiry along the same lines. Certain technical considerations had to be met at the outset of our investigations. Brock's factors are those of filtration, distance, quality of ray, and surface effect as measured in Holzknicht units, without statement as to milliamperage or time. A skin dose is a quantity effect, and a thymus or depth effect is not directly dependent on skin units, but varies with the voltage and filtration or quality (hardness) of ray. When the softer rays are used it was felt that there would be too great a disparity in the dose reaching the thymus, in a heavy boned male as compared with that in a slender female, because a relatively larger percentage of soft rays would be absorbed by the interposed tissues, and a greater error would therefore enter into the calculation of the depth dose. In studying the technic employed in Brock's cases, and assuming that a quality of ray recorded as 6 on the Benoist-Walter scale is equivalent to that obtained with a 4-inch sparkgap according to Guy, it was concluded that a harder and therefore more penetrating ray than the one employed by Brock would be desirable, because a more uniform depth effect is thus obtained.

2. Stephan, R.: *Strahlentherap.* **11**:517 (Sept.) 1920; *Munchen med. Wehnschr.* **67**:309, 1920.

3. Peterson, William F., and Saelhof, Clarence C.: *Organ Stimulation by the Roentgen Ray*, *J. A. M. A.* **76**:718 (March 12) 1921.

With the factors adopted by us—8½-inch sparkgap, 10-inch focus skin distance, 3 mm. aluminum filter, 5 milliamperes—one-half epilation dose is obtained in two minutes and forty-two seconds. This equals 1 skin unit, according to MacKee and Remer's scale. A Coolidge tube was used throughout. It may be stated here that one-half epilation dose with our factors is too large for persons of average build, and that in two minutes good results were obtained in men of large frame. In all cases the field of entry for the rays was blocked off with lead-rubber protectives and included the area from the lower border of the larynx and upper border of the clavicle to the fifth intercostal space, with the parasternal lines as lateral boundaries.

Our observations apply to twenty-three patients and extend over a period of five months. Eleven patients were given a second dose after two months, and two received a third dose. Two patients were treated too recently and are not included in this review. In all patients there had been no recent internal or external treatment which might have exerted an influence on the disease, and after the roentgen-ray treatment no internal medication, dietetic measures or local applications were employed other than as noted in the appended histories. All patients were ambulatory and followed their usual mode of life, and one had slight thyroid enlargement. No effect attributable to season was observed.

In most of the cases which responded to the treatment it was observed that within a few days the lesions had become slightly elevated and congested. The patients noticed an increase in itching, soon followed by complete disappearance of itching, which was especially commented on by those whose lesions had been habitually pruritic. After from eight to twelve days, or slightly longer, the lesions involuted rapidly; the color faded, the scales were smaller and less adherent, often resembling flour, and had lost the silvery luster, and the infiltration decreased. In the smaller lesions, however, capillary bleeding often persisted for a long time. We did not observe the rapid involution of lesions on the scalp as noted by Brock. The rapidity with which large, thickly infiltrated and heavily scaling plaques of long standing disappeared completely in four weeks was a striking feature in several cases. Central clearing was observed first in the larger patches, followed later by involution of the peripheral portion, with brownish-yellow pigmentation remaining. Patches at the elbows and knees, as a rule, proved obstinate, and remained as reddened, thin, slightly scaly spots, which condition was also observed in Brock's cases.

In one patient no response was observed, and the dose may have been too small for his age. In another the lesions grew more inflammatory, and the disorder was aggravated following the treatment; it

had not improved three and one-half months later. This patient received 0.92 skin units, which is slightly less than one-half epilation dose, but with our technic this is a larger thymus dose than that obtained by Brock. This clinical result is in accord with Brock's observation that an overdose aggravates the disorder.

Three additional cases we record as failures. In one the improvement noted could be attributed equally well to the local treatment employed. In another the dose is thought to have been too small for the patient's build, and in a third case the response was doubtful, although the patient was not seen again after the thirty-first day.

Five patients showed only a moderate or very transitory improvement, attributable perhaps to a small dosage.

In thirteen of our twenty-three cases the condition was at the least markedly improved. In eight most of the eruption disappeared entirely and only a few modified small lesions persisted, usually on the elbows and knees. In five the eruption vanished completely; these included patients with large infiltrated plaques of long standing. However, three of the five showed recurrence after varying intervals (from four to eight weeks) of entire freedom from eruption. In an early case with confirmatory biopsy the patient has been free from eruption for three months. In one instance a patient with a severe, almost universal, psoriasis was almost free from lesions in fifteen weeks and after two doses.

In all patients developing recurrence the lesions were of a milder type than those of the original eruption. They were of pinhead or split-pea size, superficial, moderately inflammatory, and frequently remained of this size and character. The recurrent lesions appeared both in previously unaffected areas and on the site of former lesions, often in the center of former plaques, and by confluence in one instance formed a new plaque. It appeared to us that there was less response by recurrent lesions to the second dose of roentgen rays than was shown by the original lesions to the primary dose. Lesions which failed to involute along with others did not appear to respond to local treatment more readily.

When considered from the patient's point of view this new method of treatment appears especially practical in that it relieves him from the time consuming use of ointments and other applications, with the attendant discomfort and inconvenience.

Without subscribing to all of the hypotheses advanced by Brock as to the underlying biologic factors involved in the response to this new procedure, it appears reasonable to us to conclude that the possibility of thymus therapy exists.

As a result of our investigations, even though the number of cases is small, we regard this method of treatment as one which produces favorable, though apparently temporary, results in a sufficient percentage of cases to justify its consideration as a practical procedure in the treatment of psoriasis.

REPORT OF CASES ⁴

CASE 1.—Louis B., laborer, aged 35, muscular, of stocky build, had had psoriasis for the past fifteen years and was never free from lesions. The present exacerbation was of several months' duration. He had received no recent internal treatment and there had been no response to ointment of ammoniated mercury applied locally. There was a generalized eruption, nummular on the extremities, with large plaques in the groins, on the trunk and lumbosacral area and a slight eruption on the scalp. There were pronounced arsenical keratoses of the palms.

Treatment: Two and one-half minutes, 0.92 skin units.

The condition was aggravated; the lesions became more inflammatory. There was no improvement after three and one-half months. He was given local treatment without response (chrysarobin, salicylic acid and ammoniated mercury).

Summary: The condition became worse, presumably due to overdosage.

CASE 2.—Arthur P., a truck driver, aged 42, a large, heavy-boned man, had had generalized psoriasis for many years; there was some improvement in the summer, with lessened pruritus. Arsenic was administered for a long time, but none had been given for the past three years. There was an extensive eruption of severe type, inflammatory, heavily scaling and pruritic. It was nummular on the extremities and scalp, with large, infiltrated plaques on the abdomen, back and sacral region. There were marked arsenical keratoses on the hands and feet.

Treatment: Seventy-four one hundredths skin units of roentgen ray was administered in two minutes. On the twelfth day there was distinct involution of all lesions. On the thirty-ninth day all lesions had disappeared entirely, including the large plaques. The patient's skin remained clear until the ninety-eighth day when there was a recurrence with guttate lesions of mild type, with slight scaling, on the trunk and extremities. On the one hundred and twelfth day (sixteen weeks) the condition was the same.

A second dose of roentgen rays, 0.74 skin units in two minutes, was administered; after eighteen weeks there was a distinct response, the scales became looser, the lesions were fading.

Summary: All lesions disappeared after five and one-half weeks. The patient's skin remained clear for a period of eight and one-half weeks. This was followed by mild recurrence which again responded to treatment.

CASE 3.—Harriet K., a well developed schoolgirl, aged 18, for the past six years had had generalized, guttate, scaly, inflammatory psoriasis, always better in summer, responding for short periods to local treatment and low nitrogen diet, with prompt recurrence. Four weeks ago there was a rapid extension in the form of an inflammatory, scaly, sheetlike pruritic eruption on the neck and upper part of the trunk, with heavily scaling, almost crusted guttate and nummular solid lesions on the extremities and scalp, which had subsided somewhat under baths, soothing emulsions and Alpine light therapy.

4. Date of observation is recorded in number of days after first treatment.

Treatment: Fifty seconds, 0.33 skin units, one-sixth epilating dose. On the tenth day, all lesions were involuting and itching had decreased. On the thirty-second day, some lesions had disappeared; the remainder were superficial and slightly inflammatory. On the forty-sixth day, the trunk had been free from lesions for a week; there were scattered guttate, noninflammatory pale lesions on the extensor surfaces of the arms and legs. The scalp was clear. On the sixtieth day there were pinhead sized discrete, scattered lesions on the chest, neck and shoulders which had been there for the past six days; other lesions were stationary.

A second dose of 0.28 skin units of roentgen rays was administered; time, forty-five seconds. On the seventieth day all lesions were fading; there were no new lesions; the trunk was clear. On the ninety-sixth day the patient reported that fourteen days ago all remaining lesions had been thick, red and scaly for several days; she was now free from lesions. On the one hundred and tenth day the eruption recurred on the arms and legs as small, superficial finely scaling, yellowish lesions. The rest of the body was clear. Six per cent. ointment of ammoniated mercury was used. On the one hundred and twenty-fourth day there was powdery scaling, not silvery, on fading, small guttate lesions, on the extensor surface of the arms and about the ankles; the rest of the body remained clear.

Summary: There was a beginning involution of a rapidly spreading generalized eruption ten days after a small dose of roentgen rays had been administered, with almost complete disappearance in six and one-half weeks. There was a recurrence of mild type after two months, with entire clearing after a second smaller dose, followed by another localized recurrence of mild type with rapid subsidence.

CASE 4.—Douglas B., single, aged 21, a skilled laborer, of tall, slender build, had guttate psoriasis which appeared on the left arm three months ago, and which became generalized within one month. There was a scaly, infiltrated, moderately inflammatory eruption of closely aggregated lesions and of patches due to confluence, most marked on the dorsa of the hands and wrists and on the thighs.

Treatment: Seven and one-half inch gap, 3 milliamperes, 12 in. focus-skin distance, 3 mm. aluminum filter, 3 minutes, 0.48 skin units. On the sixteenth day the lesions were more inflammatory. On the twenty-third day there was no change in the lesions; some new scattered lesions had appeared. On the thirty-first day the eruption was less inflammatory and the scales were loose; the condition was improving. Six per cent. ointment of ammoniated mercury was used for the hands. No later report has been received.

Summary: There was a doubtful response following a small dose; failure.

CASE 5.—Minnie B., single, aged 55, a dressmaker, of robust type, had had psoriasis twenty-five years ago, which disappeared after several years. The present attack was of five weeks' duration. She had an inflammatory, scaly, pruritic guttate eruption on the arms and legs, most marked on the elbows and knees.

Treatment: Fifty-five one hundredths skin units were administered in one and one-half minutes. On the fifteenth day the eruption was less inflammatory; there was some involution and no itching. On the thirtieth day there was a light pigmentation where the lesions had disappeared; the remainder were quiescent. On the sixty-fifth day, a few pale, slightly scaly lesions remained.

Summary: Within two months there was marked involution of all lesions and most had disappeared.

CASE 6.—Mary T., single, aged 20, a bookkeeper, well developed, had had psoriasis for three years; it became worse in the spring, affecting the arms, legs, back and scalp especially. Arsenic injections and chrysarobin had been without effect. Tonsillectomy had no effect on the psoriasis. Under a diet low in nitrogen, daily baths, roentgen rays administered locally and ointment of ammoniated mercury, she improved somewhat. There has been a recent increase in activity, accompanied by new lesions. These lesions are guttate, moderately inflammatory, lightly scaling, and elevated with a tendency to group on the trunk, shoulders, arms, legs and scalp.

Treatment: Thirty-seven hundredths skin units was given; time, one minute. On the twenty-fifth day the lesions on the scalp were less scaly. On the forty-fourth day some lesions on the neck and scalp had disappeared; all others were subsiding. On the sixty-sixth day lesions were again active on the anterior part of the shoulders and scalp. She wanted a second treatment. On the seventieth day the condition was the same. There were no new lesions.

A second dose of 0.46 skin units (with 9-inch gap) was given; time, one and one-fourth minutes. On the eightieth day the eruption was fading; there was less scaling. On the ninety-eighth day the lesions were again scaly, slightly elevated and enlarging. On the one hundred and fifteenth day the eruption persisted though it was subsiding; there was powdery scaling, and the eruption was noninflammatory.

Summary: There was involution of the eruption with disappearance of some of the lesions after six and one-half weeks; there was a recrudescence with some response to a second dose.

CASE 7.—Mrs. J. M., aged 35, a housewife, tall and spare, with large bones and a palpable thyroid gland had had psoriasis for fifteen years, with arthritis of the large and small joints of the extremities and of the spine for the past twelve years, resulting in deformity and crippling of the fingers and toes and stiffness in the back, knees and elbows. The eruption began on the scalp, and within one year it was generalized. Treatment with ointments, liquor potassii arsenitis and a low protein diet was beneficial for a time and had controlled the eruption for the past eight years. No seasonal influence was observed. About four months ago there was a marked recurrence. There was a severe and extensive eruption of inflammatory, elevated, heavily scaling, infiltrated, itching, confluent patches almost universal in type, encasing the extremities, neck and trunk, with several nummular lesions on the face. The scalp was covered with thick mortar-like scales, which extended beyond the hair margins, and to the ears.

Treatment: Forty-six hundredths skin units was administered in one and one quarter minutes. On the tenth day there was increased scaling and no itching. In forty-eight hours after treatment the patient was much more comfortable. She wanted to have the treatment repeated. On the twentieth day there were less scaling, some spells of itching and less inflammation. The scalp was clearing rapidly. The patient was given olive oil and glycerin for local application and baths. On the forty-second day many lesions had disappeared leaving a light pigmentation. The scaling was now fine and branny, not flaky, and much reduced in amount, with a granular appearance of the larger patches. The scalp was clear except in the mastoid region. On the fifty-sixth day the condition of the joints was much improved. The patient could walk, bend the back, kneel with comfort, and raise the arms to brush her hair. The lesions were light yellow, not pruritic, noninflammatory, with moderate infiltration and branny scaling. The face was clear.

A second dose of 0.46 skin units was given; time, one and one-quarter minutes. On the ninety-fourth day the scalp was clear except in the mastoid region where there were a few small lesions. The patches were clearing in the center; there was a further decrease in scaling and infiltration. On the hundred and eighth day the trunk, neck and scalp were without lesions. On the extremities there were pigmented patches dotted with pinhead size, slightly infiltrated lesions.

Summary: A severe, almost universal psoriasis, associated with multiple arthritis, showed advanced involution in six weeks, with a disappearance of most of the lesions in fifteen weeks (two doses). The condition of the joints was much improved.

CASE 8.—Anna T., aged 22, secretary, delicate, slender, had psoriasis, which began three weeks before on the extensor surface of the arms. She had split-pea sized, scaling, inflammatory lesions, showing punctate hemorrhage on scratching, on the extensor surface of the forearms and arms, thighs, upper part of the back and the anterior part of the trunk and the neck; the scalp was clear. Biopsy showed characteristic psoriasis.

Treatment: When the eruption had been present for thirty-eight days 0.37 skin units was given; time, one minute. On the eighth day, all lesions except those on the extensor surface of the arms showed involution. There was no local treatment. On the twenty-third day the only remaining lesions were on the extensor surface of the arms, and they were slightly inflammatory. On the fiftieth day there was no eruption. On the one hundred and thirty-seventh day the patient was still free from the eruption.

Summary: A patient with an early psoriasis confirmed by biopsy has remained free from eruption for three months.

CASE 9.—W. D., single, aged 26, a medical student, a muscular, heavy-set man had psoriasis which began four years ago on the elbows and knees, with later extension. No internal medication was given: chrysarobin was without effect. The eruption, which had remained in the same form for five months, was rapidly growing worse. There were nummular, pruritic, markedly infiltrated and inflammatory, heavily keratotic lesions on the elbows, forearms, thighs, knees and shins and scattered guttate lesions on the trunk, forehead and scalp.

Treatment: Seventy-four hundredths skin units were administered in two minutes. On the twenty-eighth day there was a decrease in inflammation, scaling and infiltration; the itching had disappeared. On the fifty-sixth day the condition was stationary, except for moderate infiltration.

A second dose of 0.66 skin units was administered in one and three-quarter minutes. On the ninetieth day the lesions were slightly scaly and noninflammatory, and there was a slight infiltration. The patient was given 6 per cent. ointment of ammoniated mercury and 2 per cent. salicylic acid for the hands and wrists. On the hundred and tenth day there was a definite involution of all the lesions with pigmentation, except those on the forearms and shins, where scaling and infiltration was reduced.

Summary: There was an almost complete disappearance of an actively extending eruption of moderate severity in less than four months after two doses of roentgen rays.

CASE 10.—C. G., single, aged 24, a chauffeur, a muscular, heavy-boned man, had psoriasis which began four years ago. Local and internal treat-

ment was without effect; there was no spontaneous involution at any time. He had a generalized nummular eruption with pruritic, heavily scaling, inflammatory lesions, which were most pronounced on the extremities and scalp.

Treatment: Seventy-four hundredths skin units was given; time, two minutes. On the eighteenth day he reported that eight days after treatment the condition was worse—there was more itching, inflammation and scaling. Salicylic-tar ointment was applied to the scalp, and ammoniated mercury, 8 per cent., to the trunk, with improvement, when the condition had not improved previously. The patient appeared irregularly. On the fifty-eighth day the lesions were superficial in character and moderately pruritic. The patient has not been seen since though it has been reported that he is doing well.

Summary: The response was doubtful; the treatment was not considered a failure.

CASE 11.—Frieda H., a schoolgirl, aged 16, of average size and slender, had had psoriasis since the age of 5. It was uninfluenced by the seasons and was especially severe on the scalp. Three years ago she improved for a time under low protein diet and ointments. Ten weeks ago she had diphtheria for which antitoxin was given, and four days later psoriasis appeared on the arms, then on the neck and legs. She had a generalized, guttate, nummular and gyrate, infiltrated, inflammatory and heavily scaling eruption, without pruritus.

Treatment: Three-tenths skin units of roentgen ray was administered in fifty seconds. Four months later it was reported by telephone that she was entirely well.

Summary: A generalized eruption of moderate severity disappeared after a single dose.

CASE 12.—Lucy C., single, aged 18, a clerk, a short well-developed girl, had psoriasis which began ten years ago; there were remissions during the summer. The present condition was of four months' duration, increasing in severity. There was chrysarobin staining; she had received treatment with ointments, internal medication, and been on a diet for two years without benefit. She had a guttate and nummular eruption, most marked on the back, involving the scalp, face, neck and extremities. Across the upper part of the back there was a large festooned patch. The lesions were markedly infiltrated and scaly and moderately inflammatory.

Treatment: Forty-six hundredths skin units of roentgen ray was administered for one and one-quarter minutes. On the fifteenth day there was no change. She was given 6 per cent. ointment of ammoniated mercury for the face and arms. On the twenty-seventh day the lesions were less inflammatory and scaly. She was given ointment for the trunk and scalp. On the sixtieth day there was considerable infiltration and heavy scaling, with decreased inflammation.

A second dose of 0.66 skin units was given in one and three quarter minutes. No local treatment had been given for one week previously. On the seventy-fourth day there was definite improvement, less infiltration and scaling. No local treatment had been given the preceding fourteen days. Four per cent. ointment of ammoniated mercury for the face only was given. On the hundred and fourth day there was no appreciable change. Local treatment for the face and hands with ammoniated mercury was given. On the hundred and sixteenth day many lesions had cleared in the center, and some had disappeared entirely. The condition of the scalp had improved.

Summary: Response to roentgen-ray treatment was uncertain. This case was classified as a failure.

CASE 13.—Henry S., a physician, aged 31, a well developed, deep-chested, muscular man, had had psoriasis for nine years, clearing at times in the summer, and refractory to treatment. He had infiltrated, large nummular lesions, with thick scales, chiefly on the extremities and scalp.

Treatment: Forty-six hundredths skin units was administered in one and one-quarter minutes. On the fifty-ninth day there was no change in the condition. A second dose of 0.55 skin units was given; time, one and one-half minutes. Three and one-half months later there had been no response.

Summary: This case was classified as a failure; the dose was too small for the patient's build.

CASE 14.—George H., single, aged 24, a clerk, of small stature, slender, had had psoriasis for seven months. It began on the elbows and legs, later involving the arms and trunk. He had heavily scaling, infiltrated, nummular lesions on the trunk and arms; and annular, palm-sized plaques on the legs. No previous treatment had been given.

Treatment: 0.66 skin units of roentgen ray was administered in one and three-quarter minutes. On the fourteenth day there was less inflammation and infiltration. On the twenty-eighth day there was increased scaling and pruritus. The patient was given 4 per cent. salicylic-ammoniated mercury ointment for the plaques on the legs only. On the forty-third day the condition had improved. Large patches on the legs showed pigmentation and congestion; there was no scaling or infiltration. A few small superficial lesions remained. On the sixty-first day there were no new lesions. The trunk was entirely clear, the legs showed pigmentation only; the elbows and extensor surfaces of the forearms showed a few guttate lesions. On the seventy-sixth day there was increase in infiltration and scaling of the lesions remaining on the forearms. There were several new lesions on the legs.

A second dose of 0.55 skin units was administered in one and one-half minutes. On the hundred and tenth day all lesions were pale. There was very little infiltration or scaling; there was slight itching.

Summary: In this case there was a favorable result, followed by recurrence after eleven weeks.

CASE 15.—John S., married, a laborer, aged 38, a muscular man, though slender and of spare build, had had psoriasis for nine years. He had dry, scaly, moderately inflammatory, infiltrated, pruritic patches of fused nummular lesions on the extensor surface of the arms and legs.

Treatment: Sixty-six hundredths skin units of roentgen ray was administered in one and three-quarter minutes. On the fourteenth day there was less inflammation and infiltration, but some new lesions had appeared on the legs. On the twenty-eighth day there was a complete involution of some of the lesions with pigmentary remains. On the sixty-second day the remaining lesions were noninflammatory and slightly scaly.

Summary: The eruption had practically disappeared nine weeks after a single dose.

CASE 16.—Richard P., married, aged 35, a physician, of average build, had had psoriasis for twelve years, always of inflammatory, infiltrated, heavily scaling type with nummular and palm sized lesions, with a thickened armor-like patch covering most of the anterior surface of the right shin. He had received treatment with antoserum, roentgen rays used locally, chrysarobin, ammoniated

mercury, Dreuw ointment, diet, arsenic by mouth and injection, followed by short periods of improvement; the patch on the right leg was never influenced by any treatment. There were no spontaneous remissions. For the past three years he had taken liquor potassii arsenitis at intervals without benefit, and had ceased all treatment except baths and creams until three weeks ago, when the eruption had increased in extent and severity, involving the hands and face so that treatment was imperative. There were no arsenical keratoses. There were inflammatory, elevated, infiltrated, heavily scaling patches on the trunk and extremities especially, a thick armor-like patch covering the right shin and a large infiltrated leathery plaque in the lumbosacral region. There were large and small coin-size, scaling, inflammatory patches on the hands, scalp and face. No local treatment was given.

Treatment: Forty-six hundredths skin units of roentgen ray was administered in one and one-quarter minutes. On the eighth day a decrease in scaling and redness was observed. On the fourteenth day there was marked fading of all lesions and rapid involution of the armor-like, leathery infiltration on the right shin. On the thirty-second day there were pigmentation and dryness with atrophic appearance of the skin at the site of the lesion on the right leg; all lesions on the trunk vanished leaving a light pigmentation, including the large plaque in the lumbosacral region. The hands and face were clear, the scalp slightly scaly. On the fifty-seventh day the patient was entirely free from lesions, with the exception of a few, lightly scaling, rose-red papules of pinhead size, which had recently appeared on the arms and anterior trunk. Three per cent. of ointment of ammoniated mercury was used. On the ninety-first day several pinhead to split-pea sized scattered lesions had recently appeared on the trunk and within the lightly pigmented site of former plaques on the legs. All original lesions disappeared two months before.

A second dose of 0.46 skin units was given; time, one and one-quarter minutes. On the hundred and thirty-sixth day most of the recurrent lesions on the trunk and arms had disappeared; the remaining ones were pale, noninflammatory, slightly scaling and superficial. Several recurrent lesions seen forty-five days before in the center of the original patch on the right shin persisted as heavily scaling, pea sized lesions. The scalp, face and hands were clear.

Summary: The eruption completely disappeared in five weeks, including a plaque of ten years' duration, followed in one month by a slight recurrence of mild type.

CASE 17.—Fred L., aged 42, a cashier, a heavy man with a large frame, had psoriasis which began fourteen years ago with lesions on the elbows. After one year the eruption appeared on the scalp, and two years later on the legs and trunk. The eruption was uninfluenced by treatment. It was always of the same type. There were nummular single and confluent, heavily scaling, inflammatory, infiltrated lesions on the scalp, arms and legs; there were few on the trunk.

Treatment: Fifty-five hundredths skin units of roentgen ray was administered in one and one-half minutes. Glycerin and olive oil were applied locally; 12 per cent. ammoniated mercury ointment was applied to the scalp only. On the thirty-fifth day some lesions had disappeared; the patches showed a clear center, an involuting periphery, and all other lesions thinned with little scaling, except those on the scalp, which were unchanged, and those about the left knee, where there were three verrucous patches.

Summary: There was considerable improvement of inveterate form in thirty-five days.

CASE 18.—Henry J. P., aged 63, a real estate dealer, of spare and slender build, had had psoriasis for ten years on the legs and elbows; the scalp was never clear. Treatment with ointments, the roentgen ray, Kromayer light and low nitrogen diet was ineffective. He had received no treatment for the past five years. He applied for treatment because of the good result in his son (Case 16). He had large, heavily scaling, thick congested patches on the legs, elbows and scalp.

Treatment: Three-tenths skin units of roentgen ray was given; time, fifty seconds. Fifty-eight days later the condition was unchanged. A second dose of 0.46 skin units was then administered in one and one-quarter minutes. On the hundred and third day, the condition remained unchanged.

Summary: This case was of the inveterate type with few lesions. The condition remained uninfluenced. The dose was considered too small for the age of the patient.

CASE 19.—Mrs. J. T. K., a housewife, aged 35, large and well developed, had had psoriasis for fifteen years. It became worse in the spring and had never disappeared. It always appeared in coin size, itching, scaling lesions on the trunk and extremities. During the past three months she had used 6 per cent. ointment of ammoniated mercury and had taken baths without effect. She had guttate and nummular, inflammatory, lightly scaling pruritic lesions on the extensor surface extremities, patches on the knees and elbows, patches scattered on the trunk and anterior surface of the thighs and two on the left ear; the scalp was free.

Treatment: Seventy-three hundredths skin units of roentgen ray was given; time, eighty seconds. On the fourteenth day itching ceased. There was no period of increased congestion or itching after irradiation. On the arms, scaling was reduced to a minimum. All lesions were level with the skin, pale yellow and noninflammatory, and many were smaller. On the legs the lesions were more improved than on the arms. On the twenty-eighth day continued gradual involution on the arms was seen. The lesions on the ears, trunk and thighs had almost disappeared.

Summary: There was a subsidence of the eruption in four weeks with partial disappearance.

CASE 20.—Mrs. D. K., housewife, aged, 31, slender, of spare build, thin bones, had had psoriasis for sixteen years, beginning on the elbows. It had become generalized, practically, since the onset, and was accompanied with much pruritus. There had been periods of freedom of from one to four months while she was under local treatment. The duration of the present attack was three and one-half months. There was a generalized guttate and small nummular eruption of heavily scaling, inflammatory and infiltrated, itching lesions, chiefly discrete, with fusion into small groups or patches at the elbows, knees, lumbosacral region and extensor forearms. It covered the scalp and neck, especially about the ears.

Treatment: Five-tenths skin units of roentgen ray was administered in eighty seconds. Olive oil and glycerin were applied locally. On the tenth day it was reported that after forty-eight hours itching ceased and scaling decreased. There was no further change till the eighth day when rapid fading in color

of all lesions occurred accompanied by a decrease in size and a central clearing of the larger lesions. On the covered areas the lesions were more involuted than on the neck and about the ears. The change in the eruption was very striking. On the twenty-eighth day all the lesions were fading and noninflammatory; some had disappeared entirely leaving a slight pigmentation. There was scaling in very thin lamellae. No new lesions appeared. The scalp was also clearing up and felt comfortable. Two per cent. ointment of ammoniated mercury was given for the larger lesions. On the forty-second day the lesions had disappeared with the exception of a few small papules, on which scaling practically ceased. The scalp was clear. There were no new lesions.

Summary: There was a disappearance of the generalized eruption in six weeks.

CASE 21.—Mrs. A. R., housewife, aged 34, large-boned, heavy and deep chested, had had psoriasis for thirteen years, with transitory response to roentgen rays, diet, ultraviolet light, arsenic, thyroid, baths, local applications of chrysarobin, ammoniated mercury, etc. There was a spontaneous disappearance during the summer two years ago coincident with the first four months of pregnancy; it recurred in the autumn with increased severity. Seborrheic dermatitis was associated with the condition. There were heavily scaling, almost crusted, patches on most of the scalp, especially about the ears and at the anterior margin; there was one dollar sized patch at the lower sternum, and two in the interscapular area; in each inframammary fold there was a large inflammatory and scaling, moist patch, and one similar large patch on the abdomen; large nummular, inflammatory, tender, heavily scaling lesions were scattered on the legs, thighs and extensor forearms; and on the left forearm there was one palm sized infiltrated, leathery patch. During the past ten days extension of the old lesions was observed with the appearance of new lesions, thickly scaling, and inflammatory, on the arms, legs, hands and feet, accompanied by a burning sensation.

Treatment: Forty-six hundredths skin units of roentgen ray was administered in one and one-quarter minutes. Soothing creams were applied locally. On the thirtieth day all lesions were itching, less congested, more dry, scaling thinner and smaller, and there was less infiltration. On the fifty-first day the lesions on the arms and legs were less inflammatory, less scaly and thinner; those on the chest were more inflammatory and larger. The condition of the scalp was unchanged. On the fifty-sixth day there had been an intense burning sensation in all lesions twenty-four hours before for about twelve hours, with swelling and congestion, especially of a patch on the left forearm which was subsiding; but all lesions appeared to be aggravated. On the seventy-third day there had been rapid improvement for the past two weeks and no burning or itching. All the lesions were fading; there was less scaling and the scales were much thinned. There were no new lesions; the condition of the scalp had improved, especially at the margins.

Summary: The patient had a severe, inveterate type of psoriasis with active extension, moderate initial response, acute recrudescence and improvement. Interpretation of the result is doubtful.

CASE 22.—Harry P., married, aged 30, a laborer, of average build, had had psoriasis for eighteen years in a generalized form, with improvement during the summer though the condition never cleared up entirely. Occasional treatment was given without much benefit. There was a generalized eruption of nummular

lesions, markedly infiltrated, heavily scaling, moderately inflammatory over the extremities, trunk and scalp, with inflammatory guttate lesions on the face.

Treatment: This consisted of $7\frac{1}{2}$ inches spark-gap, 3 milliamperes, 12 in. dist., 3 mm. al., 3 min., 0.48 skin units. No other treatment was given. On the thirty-seventh day there was less scaling and less inflammation of large lesions; there was no change in infiltration. The lesions on the face had disappeared; there was less scaling on the scalp. On the forty-eighth day all lesions were smaller, noninflammatory and yellowish with less scaling and infiltration.

Summary: There was progressing involution of the entire eruption in seven weeks.

CASE 23.—Arthur P., married, aged 28, a garage owner, large, heavy-boned and spare, had had psoriasis for five years as a generalized eruption, pruritic and not affected by the seasons, with at times fewer lesions. There were guttate and nummular, moderately infiltrated, scaly and inflammatory lesions on the trunk and extremities, scalp and face, of a seborrheic type of psoriasis, with larger patches on the legs, arms and midback.

Treatment: Seventy-three hundredths skin units of roentgen ray was administered in two minutes. On the twenty-eighth day many lesions had disappeared entirely with pigmentation; all others were pale, less infiltrated and free from scales.

Summary: A generalized eruption underwent almost complete involution in four weeks after a single dose was administered.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. JAMIESON, SUTTON, KILROY AND FOERSTER

DR. GEORGE HENRY FOX, New York: Just a word in regard to chrysarobin. When this remedy or its predecessor, chrysophanic acid, was introduced, it was first used in London for psoriasis with excellent results, and, as mistaken diagnoses were prevalent then as now, some cases thought to be psoriasis were cured which were really ringworm. I think Dr. Piffard and I were the first to manufacture chrysarobin in this country, by mixing goa powder with ether, and we secured excellent results. It was soon on the market and used by many. At that time, if dermatologists used even a weak ointment, it was not unusual for the patient to come around the next day or the day following armed with a club and with an extensive dermatitis. I have often wished that in place of the chrysarobin we have today we could get some of the old chrysophanic acid which was on the market forty years ago.

DR. HARVEY P. TOWLE, Boston: As a matter of record, I wish to say that, inspired by Dr. Schamberg's work, we carried out his experiments at the Massachusetts General Hospital in a series of cases with complete accord with his results. In every case of psoriasis tested the nitrogen balance was disturbed.

We found also that the reduction of the protein intake had a favorable influence on the disease. I was impressed in the course of this experience with the effect of the low protein intake. In fact, by keeping a patient on an excessively low protein diet for two or three weeks, measuring the amount carefully, and then raising the intake, we found the nitrogen balance had recovered much of its equilibrium.

Like Dr. Schamberg, we found that of itself the limitation of the diet was not sufficient to remove the disease, although in almost all instances it produced marked improvement.

DR. ERNEST L. McEWEN, Chicago: As illustrating the influence of metabolism as a factor in psoriasis, I saw recently a case in which an extensive psoriasis and a severe exophthalmic goiter began simultaneously.

As illustrating the relation of trauma to patches of psoriasis, I saw at the college clinic, within a week or two, a railroad section hand who had been a sufferer all his life from psoriasis, with many patches all over the body, two of which had never disappeared. One of these persisting patches was on the inner surface of the right knee at the point on which the pressure from the handle of a shovel would fall when it was pushed into the material to be shoveled. The other was on the outer surface of the right leg and thigh corresponding to the contact with the crowbar when the body weight is thrown upon it in the act of lifting heavy objects.

DR. DAVID KING-SMITH, Toronto: Out of a series of cases, about 800 seen while in service at the front, from March, 1915, to August, 1918, psoriasis was very uncommon. We put that down to the men's being physically fit and on simple diet. In the last two years, I have been conducting a clinic at which we see many of the same men who were formerly in the army, and psoriasis is as severe as ever with them. When they returned to the sedentary life and excesses of various kinds, the condition became just as severe.

I cannot give any suggestions about treatment, but I do know that a change has been good. We have had several of these men in the hospital, but the results have been poor. The government is willing to do anything suggested for their relief, and we have sent some of these men to a ranch, where they have invariably improved. Psoriasis was uncommon with us during the war, but is just as bad now as formerly.

DR. WILLIAM THOMAS CORLETT, Cleveland: I agree with most of the speakers that we know nothing of the etiology of psoriasis. I wholly concur with Dr. Fox on this etiologic question. I have been, nevertheless, much interested in the work of Dr. Schamberg and his co-workers, and since their painstaking experiments were published some time ago I have tried as well as I could to carry out their recommendations by restricting the protein intake, and I have kept psoriatic patients on a vegetable diet, excluding Boston baked beans, ripe peas and other substances rich in nitrogen. Many of these patients for months lived almost exclusively on a vegetable diet, but thus far I cannot say that I have been able to see any conspicuous improvement over the ordinary diet. That is the first point I wish to make, and I give it as an observation.

The second is a point alluded to in Dr. King-Smith's work at the front, which calls to mind that in southern countries with much sunlight, notably in the tropics, one sees few cases of psoriasis. In the West Indies, so far as I have observed, none are seen. In this connection, we note that the disease seldom occurs on parts of the body exposed to the sun. I once had a patient under observation who had a very copious eruption of psoriasis. His circumstances enabled him to live anywhere in the world he wished. I recommended that he go to Porto Rico. He did so and after he had been living there a few weeks the psoriasis began to disappear. During the two years he remained there he was free of the eruption. He then returned to Ohio, and the disease gradually returned. He has consulted me two or three times in the last few years, and, while his psoriasis has returned, it has never since been severe—not sufficiently severe to induce him to go to the tropics again.

In regard to arsenic in psoriasis, I have never found any special benefit from this drug except when the disease was on the decline, in which case it seems to hasten its disappearance.

DR. JAY FRANK SCHAMBERG, Philadelphia: Dr. Jamieson is to be commended for making such an elaborate study of psoriasis. I can appreciate the difficulties which he encountered. It is a most difficult matter to carry out studies on the chemistry of the blood on ambulatory patients. Furthermore, one must be extremely careful about drawing deductions unless a large series of cases is studied, because any nephritic tendency in a small group would give rise to an average increase in the nitrogen figures. If a large series of cases were studied, the disturbing effect of the inclusion of a few nephritic patients would be minimized.

Some years ago, Dr. Raiziss and I, the chemical work being done under his supervision, carried out a study on the relation of gout to psoriasis by careful observations on the purin metabolism. The patients studied were cared for in private rooms in the hospital and were placed on definite quantities of food which were determined to be free of purin content. In this manner, their endogenous uric acid metabolism was determined. They were later given food of very high purin value, such as sweetbreads, and the promptness and the regularity of the excretion of the purin derivatives was estimated. We also estimated the uric acid in the blood in a limited number of cases. After a careful study along the lines indicated we were forced to arrive at the conclusion that there was no evidence of disturbance of the purin metabolism in psoriasis.

Reference has been made by various speakers to the question of diet in psoriasis. The term "low protein diet" is a relative term. Placing a patient on a meatless diet is not of necessity placing him on a low protein diet. He may well take 12 gm. of nitrogen a day without touching meat, fish, fowl or eggs. A low protein diet in the sense in which my associates and I refer to it would represent a diet of a nitrogen content below 5 gm. a day. On such a diet, bread would be limited, cereals extremely restricted, milk allowed only in limited quantity, and meat, fish, fowl and eggs completely interdicted. It would be necessary to determine not only the quality of the food but also the quantity, as the latter naturally bears an important relationship to the nitrogen intake.

On a low protein diet the patient must live largely on green vegetables, fruits and other articles having a high caloric value but a low protein value.

Any of you may prove to your satisfaction that a diet of this character for a few weeks will exert a remarkably favorable influence on the eruption of an extensive psoriasis. My associates and I have never stated that a metabolic error was the cause of psoriasis. The question is still an open one. We do assert, however, that diet has a most important influence on the eruptive course of the disease.

We all know that psoriasis goes through various stages: eruptive activity, quiescence and spontaneous decline. No medicinal remedy either internal or external will exert a favorable influence on the disease during the course of eruptive activity. Even the roentgen ray will fail at this time. Our energies must be devoted to converting an active psoriasis into a quiescent psoriasis. There are two methods of treatment which, to my mind, are capable of bring-

ing about this change. A low protein diet and autoserum injections. When the eruption has become quiescent, it may disappear under various internal and external agencies.

The cause of psoriasis is still unknown. It may be metabolic or it may be parasitic. Future study only will determine this. One thing may be said, however: Psoriasis is a disease in which dogmatism is hazardous.

DR. SIGMUND POLLITZER, New York: I wish to say a word on the observation brought out by Dr. King-Smith that in the army he encountered very little psoriasis, but that since returning home he has seen much of it in the same class of subjects. He spoke of the simple diet of the soldier as a possible factor. While simple in quality, the diet of the soldier was extremely high in caloric value. The ration of the soldier contained about 4,000 calories a day, which is much more than an individual under ordinary circumstances could utilize. This observation, which has been made repeatedly (and the contrary observation also), illustrated the difficulty of drawing conclusions as to psoriasis. There is nothing in the world to which psoriasis has not been ascribed; and, as a matter of fact, I think we are just as far from the etiology as we were ten years ago.

As to the influence of the thymus, this work seems to me of great importance and it should be repeated on a large scale. Any assumptions in regard to the treatment of psoriasis are hazardous; but there is already a considerable series of successful results which lend probability to the utility of this method of treatment. I feel great hesitancy, however, in accepting the thymus theory, even though we might accept the fact that irradiation of the upper sternal region would affect the psoriasis. The hypothesis implies, first, a functioning thymus in the adult—which I think most physiologists would question; it implies, in the second place, that mild roentgen rays on these hypothetical thymus rests stimulate them, and that, finally, through the increased thymus function, the disappearance of the psoriasis patches may be brought about. I say these hypotheses, one planted on top of another, will require considerable further demonstration before we can accept them. But the observations are of great interest and I hope will prove of much value.

DR. ROBERT C. JAMIESON, Detroit: I was extremely interested in Dr. Foerster's observations, especially as it has been noted that the action of roentgen rays in treating psoriatic lesions, even on the neck and chest, will favorably influence lesions at a distance. The action I am unable to state, but it has been noted. I will try out the treatment to see if we can get any such results as Dr. Foerster has obtained.

I am in accord with Dr. Fox in saying that he wishes he could get chrysarobin like that of forty years ago. I have been unable to get any chrysarobin that has any action at all. The chrysophanic acid and chrysarobin are different in their action.

In regard to Dr. Schamberg's statement that we are laboring under great difficulties in making this investigation in an ambulatory clinic: We realized that there would be such difficulty in making any report on cases of this type. Our intention was to take such blood nitrogen estimations as we could get on patients in their ordinary rôle of life without making any attempt to influence them in any particular.

DR. PHILIP KILROY, Springfield, Mass.: I would like to add another remark to Dr. King-Smith's in regard to army experience. I am connected with the public health service and see many soldiers, and the striking thing to me is that many of these boys were free from everything during the war and now are afflicted with some disease. Especially is this true since the industrial depression has been so manifest; which means that they notice now what they had, but ignored, while in the army.

THE DERMATOLOGIC SYMPTOMS OF ENDOCRINE DYSFUNCTION *

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The place now occupied by the endocrine glands in medicine is of sufficient importance to affect all branches of that science, but it is particularly in dermatology that some of the phases of dysendocrinism manifest themselves. It is therefore necessary for those of us interested in this particular branch of medicine to become thoroughly acquainted with the more common surface signs of endocrine dysfunction, and it is the object of this paper to bring out the major diagnostic points of the more common of these signs as fully as possible, for on a correct interpretation depends much of our therapeutics. Unfortunately, the literature on the internal secretions is so voluminous, and its dermatologic side so little dwelt on, that the author must beg indulgence for any lapses discovered by those of his readers more skilled than he. Another difficulty encountered is the overenthusiasm of many writers on the ductless glands. The more radical French school, for instance, classifies almost every medical symptom under uniglandular or pluriglandular syndromes. The conservative and the enthusiast should remember that we are only on the threshold of knowledge on the subject and that further progress depends on working together; the issue should not be clouded by either excessive enthusiasm or complete derogation.

Interest in endocrinology was greatly stimulated by the description of exophthalmic goiter by the Irish physician, Graves, in 1835, and Basedow of Merseburg in 1840. Garrison,¹ in his excellent monograph, cites the interesting fact that more than fifty years before Basedow, Caleb Hillier Parry,² a well-known physician of Bath, accurately described the disease, and had made notes of eight cases, which were published after his death in 1825. The next great step forward was made by Addison,³ who on March 15, 1849, read a paper before the South London Medical Society in which he described the disease now

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* Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

1. Garrison, Fielding H.: Ductless Glands, Internal Secretions and Hormonic Equilibrium, *Pop. Sc. Month.*, December, 1914, January and February, 1915.

2. Parry, Caleb H.: *Collective Writings*, 2:111, London, 1825.

3. Addison: *London Med. Gaz.* 43:517, 1849.

known by his name. In 1855 he wrote a complete monograph on the subject. Pierre Marie,⁴ Charcot's pupil, was the first to differentiate acromegaly from osteitis deformans, leontiasis ossea and myxedema, and four years later associated it with disease of the hypophysis. But according to Garrison, Verga was the first to associate a lesion in the pituitary body with acromegaly. Gull, in 1873, and Ord, in 1878, described myxedema. In 1888, Sir Felix Semon⁵ showed that cretinism, myxedema and cachexia thyreopriva were one and the same. In 1889, Brown-Séquard, at the age of 72, auto-injected, subcutaneously, testicular extracts, with resulting increased muscular power and mental activity. In the same year, von Mering and Minkowski⁶ caused diabetes from experimental excision of the pancreas. These results stimulated considerable experimentation, which added much to our knowledge, but it remained for Harvey Cushing,⁷ by his brilliant experiments with the pituitary body of dogs, to show definite and positive results. He found that total removal of the anterior lobe resulted in death and that partial removal produced obesity and shrinkage of the male genitalia. Partial removal of the posterior lobe produced a temporary depression of the carbohydrate assimilation-limit, followed by a permanent increase of carbohydrate tolerance, which was lowered by the injection of an extract of the posterior lobe. More recently, considerable work has been done concerning the mechanism of correlation or inter-relationship between the various ductless glands. For example, glycosuria was produced by excision of the parathyroid glands, by injection of pituitary extract or of epinephrin and by goiter, as well as by excision or disease of the Islands of Langerhans in the pancreas. A physiologic balance readily disturbed is maintained by this correlation. Certain of the internal secretions are antagonistic, others are synergetic. For instance, "in hyperthyroidism the function of the pancreas is depressed and alimentary glycosuria is easily brought about. On the other hand, in atrophy or hyperplasia of the thyroid gland, the pancreatic powers are increased, and patients suffering from these disorders—for instance, myxedema—can take large quantities of glucose without the slightest glycosuria.⁸ The suprarenal glands, through the chromaffin tissue, stimulate the sugar-producing power of the liver and act as antagonists to the pancreas. The same glands (suprarenals) and the thyroid, mutually stimulate one another.

4. Marie, Pierre: *Rev. de med.* **11**:297-333, 1886.

5. Semon, Felix: *Tr. Clin. Soc. London*, 1888, Suppl. to Vol. 21.

6. Von Mering and Minkowski: *Arch. f. Exper. Path. u. Pharm.* **26**:371, 1889.

7. Cushing, Harvey W.: *The Pituitary Body and Its Disorders*, Philadelphia and London, 1912.

8. Harrower: *Practical Hormone Therapy*, p. 31, quoting von Noorden.

Hypertrophy of the pituitary body not infrequently follows atrophy of the thyroid. Foerster,⁹ in an excellent paper read before the thirty-ninth annual meeting of the American Dermatological Association, calls attention to a correlation of special interest to the dermatologist—that existing between the sympathetic system and the ductless glands. He states that

The connecting link is found in the chromaffin tissue, which is widely distributed—in the medulla of the adrenals, in the sympathetic ganglia and plexuses, aortic and carotid bodies, prostate, ovary, kidney and ureter. This chromaffin system is intimately allied to the sympathetic system in embryologic derivation and in location, and through its secretion has a specific action solely on tissues innervated by the sympathetic system, that is, on nonstriated muscle fibres. This tissue, under normal conditions of secretion, is thereby kept in a normal state of tone. If the adrenal tissue is defective or excessive, there is a corresponding loss or pathologic increase of sympathetic tone. The action of adrenin is on sympathetic end-mechanism, and not on centers, and its action is antagonized, neutralized, or compensated by other substances, normally produced in the organism, such as cholin, which act preferably on the autonomous or aprasympathetic system. Through their sympathetic nerve supply, the other organs of internal secretion are subject to control by the internal secretion of the chromaffin system. For example, the thyroid is supplied with vaso-constrictor and vaso-dilator nerves, and on these, whichever is the sympathetic group, adrenin has a stimulating action. Similarly, an intimate relation is known to exist between the adrenals and the pancreas.

This association of the sympathetic and the ductless gland system may account for the group of angioneurotic dermatoses, such as symmetric gangrene, scleroderma, angioneurotic edema and dermatographia. The pathologic changes in the skin, associated with disturbances of the internal secretions, are so many and varied that it were best to treat them under separate headings.

SYMPTOMS

Dermatologic Symptoms Dependent on Errors in the Pituitary Secretion.—These are well summed up by Cushing,⁷ as quoted by McEwen.¹⁰

In Hyperpituitarism: The symptoms are: increase in the size of the hair follicle; hypertrophy of the papillae; enlargement and activation of the secretory glands, causing a moist and greasy skin; increase of connective tissue in the subcutis giving the skin a dense, boggy feel, with increase of depth of the furrows of the hands and face; hypertrichosis.

9. Foerster, O. H.: The Relation of Internal Secretions to Cutaneous Disease, *J. Cutan. Dis.* **34**:1 (Jan.) 1916.

10. McEwen, E. L.: The Relation of Internal Secretions to Cutaneous Diseases, *J. Cutan. Dis.* **34**:15 (Jan.) 1916.

In Hypopituitarism: The symptoms are: smooth, transparent skin, free from moisture, almost infantile in character; failure of axillary and pubic hair, with feminine distribution of the latter in males; thinning of the hair of the scalp when occurring in adult life. Pigmentation is often a conspicuous feature.

To the foregoing may be added the state described by Fröhlich¹¹ and named by Bartels dystrophia adiposogenitalis and characterized by an excessive adipose development, stunted growth, deficient sweat, dry skin, dry strawlike hair, and in the male, shrunken, undeveloped genital organs. The author has lately observed a male adolescent with the typical Fröhlich syndrome, who had a classical pityriasis rubra pilaris. There was slight improvement in the eruption after administration of pituitary extract.

Dermatologic Symptoms Dependent on Errors in the Secretions of the Pineal Body.—The pineal gland, a small pinkish body situated beneath the posterior region of the corpus callosum, and resting on the anterior elevation of the corpora quadrigemina, is not of much dermatologic interest. Ogle,¹² Gutzeit,¹³ Oestreich and Slawyk,¹⁴ and Frankl-Hochwart¹⁵ have described a peculiar syndrome occurring in young subjects suffering from disease of the corpora quadrigemina and involving the pineal gland. This syndrome consists of an excessive and abnormal growth of hair, associated with premature sexual and genital development and abnormal height. The genital enlargement is such that boys of 7 and under, suffering from this disease, exhibit a penis of adult size. These symptoms, according to Swale,¹⁶ are supposed to be due to a hypofunction of the pineal gland. Pellizzi¹⁷ has called this pineal syndrome macrogenitosomia praecox. On the other hand, Howell¹⁸ states that Dandy has completely removed the pineal gland in dogs with no untoward after results, the animals remaining under observation for over a year.

Dermatologic Symptoms Dependent on Errors in the Secretions of the Parathyroid Glands.—These glands are still the subject of much controversy, one school believing that they are part of the thyroid,

11. Fröhlich: Wien. klin. Rundschau, 1905.

12. Ogle: Tr. Path. Soc., Lond. **50**: 1899.

13. Gutzeit: Dissertation, Königsberg, 1896.

14. Oestreich and Slawyk: Virchows Arch. f. path. Anat. **162**:475, 1899.

15. Frankl-Hochwart: Deutsch. Ztschr. f. Nervenhe. **37**:455, 1909.

16. Swale, Vincent: Internal Secretion and the Ductless Glands, London, Edward Arnold, **20**:464, 1912.

17. Pellizzi: Riv. ital. di neuropatol. ed elettrotet. **3**:193, 1910.

18. Howell, William H.: Physiology of Secretion, Reference Handbook of the Medical Sciences, New York, William Wood & Co., **7**:703, 1917.

that they are an embryonic and partly developed thyroid tissue and that they are not separate structures. This was Gley's original belief. Another school claims that these glands have an entirely different function than the thyroid gland and in some way control calcium metabolism. In support of this theory of separate function is the case reported by Hertz¹⁹ in which a man of middle age, from whom the thyroid gland had been removed in greater part, developed a tremor, after remaining well for a few years. His hair ceased to grow, his weight rapidly decreased, he suffered from diarrhea and became impotent. Thyroid extract aggravated the trouble. After taking dry ox parathyroid by mouth for six months, all of the symptoms disappeared.

Dermatologic Symptoms Dependent on Errors in the Secretions of the Thyroid Gland.—The two most important pathologic changes in this gland, as far as the skin is concerned, are those accompanying exophthalmic goiter and myxedema. The cutaneous symptoms accompanying exophthalmic goiter are unfortunately not specific, and are only a part of the general syndrome. They consist of a marked hyperhidrosis, particularly axillary, transient erythemas, hyperkeratosis palmaris et plantaris, pruritus, urticaria, dystrophy of nails and hyperpigmentation. Hyde and McEwen²⁰ in an analysis of 111 cases of exophthalmic goiter, found that forty-nine patients had hyperhidrosis, fifteen had pigmentary changes and five had scleroderma. Among the rest, a considerable number suffered from extensive alopecia, urticaria, leukoderma and transient erythemas. Sabouraud believes that chronic alopecia is occasionally brought on by hyperthyroidism.

In myxedema there is a swelling of the skin, most noticeable about the chin, lips, nose and cheeks. This swelling resembles fat, but on palpation has a softer feel and is more elastic than fat. Unlike ordinary edema, it does not pit on pressure, nor does any fluid exude when the skin is pricked. The skin is dry, rough and cold; at a later stage it may become yellowish in color. Verrucae and nevi, with or without pigmentation, may appear. Perspiration may be entirely absent. Tumefactions in the supraclavicular regions are frequently noted. The hair is thin, dry and scanty. The head at times is almost bald, and the skin of the scalp is dry, brown and scaly. The hair is frequently prematurely gray. The eyebrows are scant, particularly at the outer third, and the pubic and axillary hair may disappear entirely. Changes in the nails and teeth also occur. The mucous membranes of the mouth and nose are swollen and very dry. According to Foerster, "The myxoedematous

19. Hertz: Practitioner, London, special number **94**: No. 1 (Jan.) 1915.

20. Hyde and McEwen: Am. J. Med. Sc. **125**:1000, 1903.

skin discloses a peculiar degenerative process in the cutis, with changes in the elastin and collagen elements. The elastic fibers are swollen, the collagenous bundles are attenuated, or may almost disappear, and both are transformed into a homogeneous hyaline-like mass. An obliterating endarteritis is also observed, which is similar to that found in the atrophic thyroid gland. The epithelium of the coil and sebaceous glands is swollen and proliferates, and occludes the lumen of the glands." A relationship between the diseased thyroid and the pathologic condition, termed *adiposis dolorosa*, or Dercum's disease, is believed by many to be existent. This condition is characterized by various sized, circumscribed, painful, fatty, connective tissue tumors, most frequently situated on the arms and legs. There is also an accompanying general obesity. The flesh bruises easily with resulting frequent ecchymoses. Trophic changes in the form of ulcerations, blebs and bullae have been observed. Foerster states that pathologic changes in the thyroid were discovered in five out of six cases at necropsy. Price,²¹ in an analysis of eight necropsy examinations, found that disease of the thyroid gland was present in seven cases. The reports of Singer,²² Notthafft,²³ and Hektoen and Wells²⁴ seem to prove some relationship between dys-thyroidism and scleroderma; the two conditions are too frequently correlated to be accounted for by mere coincidence. The successful therapeutic use of thyroid extract in scleroderma, though not invariable, is still frequent enough to add to the etiologic evidence. Ichthyosis may also reflect thyroid disturbance. Winfield²⁵ reported a case of fetal ichthyosis in a child that died at the age of 2½ weeks. At necropsy no thyroid gland was found. Several other cases of ichthyosis with thyroid disturbances have been reported. Symmetric gangrene (Raynaud's syndrome) has been ascribed by some writers to subthyroidism. Many other dermatoses have been claimed to be caused by disease of the thyroid gland, but corroborative evidence is as yet very slender.

Dermatologic Symptoms Dependent on Errors in the Secretions of the Thymus Gland.—No connection between disease of this gland and the skin has yet been demonstrated. Macleod²⁶ believes that through its action the scalp is made susceptible for the growth of the ringworm fungus.

21. Price: *Am. J. Med. Sc.*, May, 1909.

22. Singer: *Berl. klin. Wehnschr.*, 1895, p. 226.

23. Notthafft: *Centralbl. f. Allg. Path.*, 1898, p. 870; *Centralbl. f. Inn. Med.*, 1898, p. 353.

24. Hektoen and Wells: *J. A. M. A.* **28**:1240, 1897.

25. Winfield: *J. Cutan. Dis.* 1897, p. 516.

26. Macleod: *Practitioner*, London, February, 1915, p. 298.

Dermatologic Symptoms Dependent on Errors in the Secretions of the Chromaffin System.—This system, next to the thyroid the most important of the human organism, comprises the chromaffin tissue, the suprarenal and the carotid and coccygeal glands. Its best known and most interesting disease, in a dermatologic sense, is that bearing the name of Thomas Addison, the cutaneous manifestations of which are clearly cut, consisting mainly in a melanoderma of varied degree, both as to its onset and intensity. The pigmentation usually appears at a later stage in the development of the disease, but occasionally it may precede all other symptoms, as evidenced by a case reported by Greenhow, in which the dyschromia preceded by eight years the other symptoms of Addison's disease. Rarely the disease runs its course without dermatologic evidence. At times the pigmentation is so slight that it escapes notice. Henry²⁷ states that Bramwell exhibited a patient at the Edinburgh Royal Infirmary, whose chief symptoms consisted of moderate anemia, emaciation and extreme prostration. The case was presented for diagnosis. On walking away to put on his clothes, the patient passed through an area of unusually good light, and it was immediately observed that he had two or three pale, brownish, discolorations over the dorsal vertebrae. He was recalled, and on the inner left cheeks was found the typical addisonian discoloration. The degree of pigmentation varies from almost the black of a dark negro, to a faint tan. The pigmentation is usually an exaggeration of the normal, and occurs mostly in parts normally pigmented, namely the areola around the nipples, the genitals and groins, the extensor surface of the forearms and the axillary folds. The melanodermic areas are not sharply margined, and friction or pressure increases the pigment. It is usually first noticed on the face, neck, and the backs of the fingers and hands, especially over the joints. The linea albicantes may become dark. As a rule, the palms and soles are not affected. On the other hand, Rolleston²⁸ observed two cases of pigmentation of the palms, with intensification of the various lines. In some cases small mole-like specks, as black as ink, may be observed scattered over the body. The mucous membranes are also involved, the discoloration occurring on the tongue, at its free border, the inner cheeks and the gums. It is accentuated by any local irritation, such as a jagged, carious tooth. The discoloration has been compared to that occurring after eating blueberries or blackberries. The hair sometimes becomes darker. Sargent's sign, which consists of a white line appearing on the skin of

27. Henry, Frederick P.: Addison's Disease, Reference Handbook of Medical Sciences, New York, William Wood & Co. 1:114, 1917.

28. Rolleston: Allbut's System of Medicine, London, 4: 1901.

the abdomen when lightly rubbed with the finger, is frequently present. The etiologic pathogenesis of the pigmentation is not definitely settled. McEwen advances two theories:

(1) That the physiologic pigmentation is greatly increased by an increase in the number of chromatophores. Presumably these cells are under the control of the sympathetic system, which in Addison's disease is at fault.

(2) That the matrix of adrenalin is found in tyrosin, and allied products of proteid decomposition; that in disease of the suprarenals, adrenalin is no longer elaborated from the mother substances. These accumulate in the tissues, and in the skin, especially where exposed, are converted by oxydases (tyrosinase) into a dark colored pigment body of the melanin group.

Microscopically, the pigment is deposited in the cells of the rete malpighii, in contact with the papillae. It rarely appears in the corium, although at times pigmented, and branched connective tissue cells are found.

Darier²⁹ believes that the melanodermas in Addison's disease, chloasma, acanthosis nigricans, and perhaps the pigmented syphilids, have an analogous pathogenesis. Neurofibromatosis may be related to hypofunction of the suprarenal glands. A diffuse pigmentation frequently accompanies the tumor formation. Oddo and Jullien noted pigmentation of the mucous membranes in three cases of Recklinghausen's disease. Pic and Jullien report three cases of the disease in which suprarenal treatment was followed by an immediate and marked improvement. Chauffard and Brodin secured a notable improvement from the administration of suprarenal tablets in a man, 32 years of age, with diffuse pigmentation, low blood pressure, and forty rather symmetrically arranged subcutaneous fibromas.

The pancreas is of interest to the dermatologist because of its relation to hyperglycemia and glycosuria, with resulting anhidrosis, pruritus, perforating ulcer of the foot and other dermatologic symptoms related to diabetes.

Secretin, the name given to the internal secretion of the intestinal mucous membrane, whose function it is to stimulate the external secretion of the pancreas, is not of dermatologic interest. A similar secretion is formed in the pyloric portion of the gastric mucous membrane, whose function it is to stimulate the secretion of gastric juice. Hyperfunction of this secretion might very well cause hyperchlorhydria, with resulting acne rosacea, recurrent herpes labialis and other dermatoses related to gastric hyperacidity.

29. Darier: *Textbook of Dermatology*, Ed. by S. Pollitzer, Philadelphia, Lea & Febiger, 1920, p. 324.

The gonads are of tremendous importance in general medicine. Their apparent control of pilosis makes them extremely interesting dermatologically. Removal of the male gonads results in scanty hair growth. In the female, their removal often causes hypertrichosis. Lowered activity of the gonads in old age is accompanied by atrophy of the skin and thinning of the hair. The relationship between ovarian dysfunction and hypertrichosis is well known. In an article on the subject, the author³⁰ reported 146 cases of hypertrichosis, in which eighty patients were found to have serious menstrual disturbances, but fully 25 per cent. of the remaining sixty-five patients had minor anomalies of menstruation. Another interesting point brought out was that normal sexual life seemed to inhibit hirsuties. Of the 146, 106 were unmarried. Of the 106 single women, only four were less than 18; in all four puberty was well established. The ovary, however, is not alone responsible. There is an intimate relationship between it, the suprarenal, the pineal and occasionally the pituitary body, so that hypertrichosis is frequently the result of a disturbed pluriglandular equilibrium.

COMMENT

This brief and incomplete review of the subject shows how much is yet to be learned. It may well be that the future will see the etiology of a number of dermatoses cleared up by rigid and conscientious study and experimentation in the field of endocrinology, for as yet, in spite of many discoveries, we are really only on the outskirts of that promising field. I have purposely omitted descriptions of the so-called "types" of endocrine dysfunction, for while prepared to admit that such characteristic markings do exist and can be classified, I cannot as yet be led to believe that a few freckles and thick eyebrows denote the suprarenal type, or that a smooth blond skin with scanty eyebrows denotes the thyroidal type. It is in such minutiae that one becomes lost in the realms of fancy.

ABSTRACT OF DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: Without in the least wishing to minimize the importance of Dr. Bechet's contribution, I think we should at least inject a word of warning as to the very loose use of the words "endocrine dysfunction." We are just on the threshold of knowledge concerning the relation of the disorders of the endocrine glands, so-called, and the various dermatoses. Perhaps, in the future we shall be able to correlate certain obscure dermatoses into causal relationship with various disorders of the endocrine glands. The fact remains, however, that today, notwithstanding all speculation, very few cutaneous diseases are due to definitely known endocrine disturbances.

30. Bechet: *Etiology and Treatment of Hypertrichosis*. New York M. J. Aug. 16, 1913.

The well-known changes of the thyroid, and the hypothyroid disturbances, the diseases associated with the suprarenals, and the physiologic and pathologic changes resulting from emasculation in both sexes, practically sum up all we know about endocrine dysfunction, and a warning is timely. We have all influenced cases of scleroderma by the administration of thyroid extract, but that is no proof that the scleroderma is due to endocrine dysfunction, so-called. I have been able to clear up a case of pityriasis rubra pilaris by the empiric use of thyroid, but I certainly would not be justified in stating that this disease is a result of endocrine dysfunction, so-called. I think until we have much more information we should consider that these are merely accidents, empiric accidents, and until we are in possession of more definite knowledge of the endocrine system we should be careful about the too loose use of the term "endocrine dysfunction."

DR. LESTER HOLLANDER, Pittsburgh: The intricate interrelation of the endocrine glands through the agency of the sympathetic nervous system makes the approach of this subject difficult, for when the clinical syndrome of one of the endocrine glands is considered, the entire system must be taken into consideration. If this correlation can definitely be separated, and if we can lay our fingers on definite changes in the different endocrine glands, it is of the greatest interest. I do not consider endocrinology a panacea for all obscure dermatologic conditions, but I do believe that the relation of the endocrine glands to dermatoses of a metabolic nature is of great importance. The dermatologic syndromes as described by Dr. Bechet do not need any elucidation. We must utilize all the subjective and objective symptoms which can be elicited, and all such procedures as basal metabolism tests, determination of hyperglycemia, the use of the roentgen ray for the determination of the sella turcica and the appearance of the bony structure of the skull, the utilization of the signs which have been described definitely as due to conditions of hyperthyroidism or hypothyroidism or dyspituitarism; in other words, the study of the patient as a whole may bring some definite light. It is true that we meet with dermatoses in cases of hyperthyroidism which are not due to the hyperthyroidism per se, but by paying attention to the coexisting thyroid condition, the dermatologic condition can also be improved. Endocrine therapy leads us into a polypharmaceutical forest, the exit from which, at times, at least, is very difficult. It will be of considerable help when the basic factors in endocrinology are better understood, and therefore I agree with Dr. Wile in his remarks regarding the indiscriminate use of thyroid as it is provocative of bad results at times. I have had a good deal of experience in the use of suprarenal gland substance, and a word of caution is necessary to those who are not familiar with its action, that is, in all cases in which this is administered, the blood pressure should be observed carefully from time to time for hypertension.

DR. ERNEST L. McEWEN, Chicago: I have been particularly interested in the possible relationship of the endocrines to hypertrichosis, and while I have made many observations, I cannot say that I have arrived at very positive conclusions. The relationship of the gonads to hypertrichosis is shown in the case of a married woman with a mild hypertrichosis who reported that since 1917 she had passed through two pregnancies and lactation periods during which the facial hair growth had remained entirely quiescent; it was now again becoming active.

DR. FRED WISE, New York: Dr. Bechet mentioned the case of a patient being successfully treated for pityriasis rubra pilaris with thyroid extract. Dr. Wile reports likewise. That does not prove that this disease is due to thyroid disturbance, but it does suggest that, perhaps, the next twenty patients will be cured by the same means. Cases of dermatitis herpetiformis and molluscum fibrosum have been described as due to thyroid troubles, and these patients should be sent to an endocrine expert who knows what to give and when to give it.

DR. PAUL E. BECHET, New York: The object of the paper was three fold; to summarize what was definitely known of the interrelationship between the ductless glands and the skin; to bring forth some discussion from those with wider experience in endocrinology; to avoid fanciful and unproved theories.

THE ROENTGEN-RAY TREATMENT OF ACNE VULGARIS *

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During the past six years we have treated a number of patients suffering from acne by the modern roentgen-ray technic. One hundred and seventy cases have been followed carefully enough to be reported. All of these were private patients and all were watched as carefully as possible. During the war, Washington had a floating population and the result naturally is that we have lost sight of many persons and are unable to give the permanent results in these instances.

Beginning with the year 1900, numerous reports concerning the use of the roentgen ray in acne began to appear in the literature; many of these references are given by Pusey and Caldwell.¹

At first treatments were given at short intervals according to the old divided dose technic. However, within the last six years, thanks largely to MacKee's pioneer work in America, the doses have been measured, and hence the intervals between treatments have been lengthened.

TECHNIC OF TREATMENT

At the beginning we treated our patients every three weeks with the following technic: spark gap $7\frac{1}{2}$ inches, milliamperage 4, time forty-five seconds, focal skin distance 9 inches, no filter. This is three fifths of the dosage employed in epilating the scalp for ringworm. However, we soon learned that some blondes would show a slight erythema after such a treatment, so for the past two years we have been using the following technic: spark gap $7\frac{1}{2}$ inches, milliamperage 4, time thirty-five seconds, focal skin distance 9 inches, no filter, doses given at intervals of two weeks.

* Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

1. Pusey and Caldwell: *The Practical Application of the Roentgen Rays in Therapeutics and Diagnosis*, Ed. 3, Philadelphia, W. B. Saunders & Co., 1904, p. 367.

Since adopting this technic we have not had a single case of erythema. The facial acne exposures were given to both sides of the face and to the forehead. When the temples are affected, exposures are given to both of them, care being taken that the angle of incidence is 90 degrees from the exposures given to the forehead. The eyes, eyebrows and hair are protected with heavy lead rubber. At times it is necessary to treat the bridge of the nose and the area between the eyebrows. When the back or chest is treated we use the same technic, except that the time is increased to forty-five seconds. Because of our relapses, which will be discussed later in the paper, we now recommend that patients be kept under observation for at least one year. While we fully realize that each person is a law unto himself, the average course of treatment which we outline is as follows: from six to eight treatments at intervals of two weeks, then two to three treatments at intervals of three weeks, and then one treatment each month or six weeks for the remainder of the year.

At times we find that the skin becomes very dry from the use of the roentgen ray. When this occurs, we recommend a simple ointment consisting of 10 grains of sulphur to the ounce of white petrolatum or cold cream.

In addition to the roentgen-ray treatment, the patients are advised to live hygienic lives, to keep the bowels open, to eat no chocolate, and in many instances to reduce the carbohydrate intake. As a rule, we do not find it necessary to express comedones as they usually dry up and drop out by the fifth treatment. The results of treatment are shown in Table 1, and Table 2 will show how promptly the improvement took place.

RELAPSES

In our series of cases we know of thirty-nine instances in which there was a relapse. These have varied in time from two months to eleven months after treatment was discontinued. In only three instances was the relapse as bad as the original condition. It should always be remembered that it is normal for young persons to have two or three acne pustules at least once a month. This, of course, is particularly frequent about the time of menstruation in women. Some of our patients who have complained of relapses have had no more lesions than these monthly, even though they had a bad acne when treatment was commenced. We have not felt it proper to consider such cases as definite relapses, but simply as showing normal physiologic conditions. Of our patients who did have a relapse, fourteen had a relapse after a course of eight or more treatments. In the other twenty-five cases, the number of treatments received varied from three to six.

In view of the facts just mentioned, we feel that a patient should receive a full course of treatments as previously outlined.

FAILURES

In seven instances we were not successful in producing beneficial results. In three of these instances patients discontinued treatment after less than five treatments. In two other cases there was some temporary improvement, but the disease could not be held in check by the ordinary technic. We have been careful to exclude the cases of rosacea, for we have not been nearly so successful in treating this condition as we have been in treating true acne vulgaris.

TABLE 1.—RESULTS OF TREATMENT OF ACNE VULGARIS BY THE ROENTGEN RAY

Results	Papulo-				Total
	Juvenile	Pustular	Indurata	Back	
Improved		17	3		20
Cured	2	41	20	4	67
Cured, bad relapse		3			3
Cured, mild relapse	3	28	5		36
Cured, question as to relapse.	2	26	6	3	37
Failures		6	1		7
Totals	7	121	35	7	170

TABLE 2.—NUMBER OF DOSES OF ROENTGEN RAY NECESSARY FOR IMPROVEMENT OR CURE IN CASES OF ACNE VULGARIS

No. Doses	Juvenile	Papulopustular	Indurata	Back	Total
1		13	6	2	21
2	2	32	10	3	47
3	4	39	11	5	59
4	1	22	4		27
5		5	3		8
6		1	2		3
7		2			2
	7	114	36	10	

COMPARISON WITH OTHER METHODS OF TREATMENT

A large number of our patients who were cured with the roentgen ray had failed to respond to the older methods of treatment. In at least one half of our cases, we had given the following well-known methods of treatment a thorough trial: regulation of diet and bowels; thorough use of astringent lotions; plenty of soap and water; expression of comedones, and the use of arsenic internally. From our experience we are convinced that such a course will not benefit more than one third of the cases in which it is tried, unless it be kept up for a long period of time.

Thirty-eight of our patients had had vaccines used. The majority of these report temporary good effect, but no lasting benefit. The present fad of using yeast in the diet had failed to work in at least thirty instances. Hence we naturally feel that we can obtain better and quicker results with the roentgen ray than with any other method. That the patients feel the same is evidenced by the fact that at least two thirds of our patients are sent in by those who have undergone this treatment.

COMPLICATIONS AND SEQUELAE

The most serious complications that can follow overdosage in acne are telangiectases and atrophy. In four instances patients had telangiectases as the result of treatment. In one case this was due to a deliberate overdose given in an otherwise successful attempt to cure the worst case of acne indurata that we have ever seen. In another instance, telangiectases occurred over the lips and chin. This patient had received previous roentgen-ray treatment, and as a result of our first treatment this area became very dry. During all other treatments the area was shielded with lead rubber, but nevertheless these unpleasant sequelae resulted in about a year. In a third cases a few telangiectases appeared on the arms, which had received exposures of from 45 to 50 seconds of time each when treated. In a fourth case a few telangiectases appeared on the nose. This last case is particularly interesting because no treatment of more than twenty-five seconds was ever given, and yet in one or two instances there was a slight reaction. One case which showed no telangiectases showed some atrophy. In this instance the protecting lead foil slipped so that a double dose was received over a limited area on the upper part of the cheek. In one case there had been an unpleasant amount of permanent dryness, so that the lines at the corner of the mouth were accentuated. Despite this dryness, an occasional pustule still appears.

It is not at all infrequent that, as a result of its becoming dryer than is normal, the skin will be easily irritated by wearing apparel, or by too frequent use of soap and water. A large number of our cases have shown this complication at times, but we have had no difficulty in controlling it by means of a simple ointment.

Freckles frequently appear a few weeks after treatment is begun. Some brunettes show a marked temporary pigmentation. This is usually of not more than two weeks' duration; but in one or two instances a slight amount of pigmentation around the corner of the mouth has persisted from three to four months.

One of the most serious criticisms that have been made regarding the roentgen-ray treatment of acne is that it will produce deeper pits owing to the fact that the scar tissue is supposed to be absorbed by

the rays. We have watched all of our cases carefully, and it is possible that in three instances the pits were deeper than they would otherwise have been, but we are not certain that this is true. As a matter of fact the amount of treatment given to an acne lesion would not have any influence on a hypertrophic scar, and it is rather difficult to see how the scar tissue in the acne lesion could be affected. Alopecia will not result from this treatment as the hair is always carefully protected.

A number of patients have felt that roentgen-ray treatment stimulates the growth of superfluous hair. We do not believe that this is possible, for several reasons. First, superfluous hair and acne travel hand in hand, both being an abnormal condition of the pilosebaceous gland apparatus. Second, the growth of superfluous hair is usually most marked directly under the chin, where practically no treatment is received.

Howard Fox² reports highly satisfactory results in forty cases, with only two cases which could rightly be called failures. Witherbee and Remer³ have likewise reported excellent results, stating that they have had practically no recurrences.

CONCLUSIONS

The use of the roentgen ray in acne is highly satisfactory in the majority of instances, the results being quicker and more permanent than with any other method of treatment. However, it must always be remembered that the roentgen ray can do damage and that we must be extremely cautious in order not to give an erythema dose.

ABSTRACT OF DISCUSSION

DR. RICHARD L. SUTTON, Kansas City, Mo.: Dr. Grover Wende told me that in a recent conversation with Dr. Coolidge he had been informed by the latter that despite all they could do in the matter of standardization, unscreened tubes sometimes varied as much as 50 per cent. While we all agree that the Coolidge tube is by far the best that can be procured at this time, and while it may be safe for experts to treat acne with the roentgen ray as a routine method, I hold that the average man had better leave this method of treatment alone. Every now and then I see an extremely disastrous result following even presumably careful applications. Even when everything is taken into consideration, the greatest care and prudence must be exercised if atrophy and other unfortunate sequelae are to be avoided. I have found that an accompanying focal infection is one of the most common of all causes of chronicity in these cases, and that the removal of the focal infection will often effect a cure when all other measures fail.

DR. EVERETT S. LAIN, Oklahoma City, Okla.: In 1912, Dr. Varney read a paper on vaccine treatment of acne. In discussing his paper I had advocated roentgenotherapy as a more satisfactory method. I recall the quite severe

2. Fox: *J. Cutan. Dis.* **35**:599 (Sept.) 1917.

3. Witherbee and Remer: *Med. Rec.* **99**:482 (March 19) 1921.

criticism of the roentgen-ray treatment of acne which I started. After having used roentgenotherapy for a number of years in the treatment of acne, even during the early days of unmeasured dosage, the harmful results were so slight as compared with the uniformly good, that I continued this method. Especially is this true in the extremely stubborn cases which have resisted medicinal and other treatment. During the past few years, since dosage can be measured so accurately, any one can master the technic so as not to endanger the skin in the treatment of ordinary cases. I use one-half skin or erythema dose for the first treatment. I also look after free elimination by all of the excretory organs. Focal infections are carefully watched for and removed if found. Dr. Sutton called attention to the variation in degree of activation from roentgen-ray tubes. Dr. Coolidge declared that 1 mm. of filter largely corrected this variation, thereby proving that the difference was mainly due to difference in consistency of the glass.

DR. FRED WISE, New York: I can look back on eight years' experience without the roentgen ray and to eight years with the measured doses of roentgen rays. In my opinion the method is perfectly safe if one knows how to use the roentgen ray. The whole question is whether the man is capable of giving roentgenotherapy properly. If he is, there will be no trouble. No cases have come to our notice in which bad results—telangiectasia around the chin, etc.—have occurred following the use of this method. In the opinion of MacKee and Remer, who have had an enormous amount of experience, the best dose is one-fourth unit, skin distance once a week. The question of how many successive doses should be given is also rather arbitrary. We have had cases in which ten or twelve treatments and more were given without bad results. These treatments were given many years ago, and the patients have been observed for other conditions since that time, without seeing any bad results. An examination of the patient in a light room should be made after each exposure. Physicians who practice in dark rooms, or receive their patients at night time or by electric light, are likely to overlook an area of erythema around the eyes. If this area is overlooked, these patients are likely to get into trouble from overtreatment. The treatment should not be repeated until the erythema has subsided entirely. I wish to corroborate what Dr. Hazen said about freckling. This is certainly true in New York, particularly in brunettes, and it is exceedingly annoying to the patients, but it is only evanescent. One question that frequently comes up is whether to use some external applications in conjunction with roentgenotherapy. In cases that are resistant even to roentgenotherapy I have tried a mild lotio alba without getting any ill effects, and it hastens the cure. With regard to the pitting, that is more or less a psychologic matter. Many patients come in with pits due to the acne itself, and they are made more prominent by the disappearance of the acne lesions. From my experience, roentgenotherapy has no causal effect on this pitting, but when you clear up the acne, the pits which were there long before the acne was cured are more conspicuous, and the patients are dissatisfied when they see these blemishes.

DR. WILLIAM H. GUY, Pittsburgh: In the treatment of acne vulgaris the treatment must be divided between treating the patient himself and treating the disease. Dr. Sutton raised the question of uniformity of energy output from the Coolidge tube over a certain length of time, and stated that a 50 per cent. variation may occur. There may be such theoretic objections, but the experience of MacKee and others has shown that there is no such variation.

A large number of scalps have been epilated using the Adamson-Kienböck technic and MacKee's system without a radiometer. The margin of safety in this work being 25 per cent., and permanent depilation not being met with, it seems to me that from a practical standpoint a 50 per cent. variation does not exist. The results obtained in the treatment of acne are necessarily dependent on accurate dosage and on never producing an erythema. I agree with Dr. Wise that the pits that are seen and so frequently ascribed by patients to the roentgen ray can with better grace be credited to the disease itself. Many cases of acne respond beautifully, some with pits and some without marked pitting. Results vary with the severity of the case.

DR. WILLIAM ALLEN PUSEY, Chicago: I agree with practically all that has been said, although on some details I have my own views. For twenty years I have been treating acne with roentgen rays and I consider it the one effective method. I divide my cases into two classes: those that I treat with roentgen rays and those that I do not. Those that I do not treat I consider so trivial as not to make roentgenotherapy necessary. The other cases I treat with roentgen rays and know of no other way of getting them under control. I do not treat certain cases because I feel they do not warrant this important procedure. Because the treatment of acne with roentgen rays is the test of one's capacity to use roentgenotherapy, it should not be undertaken until one is sure of himself and of his apparatus. The severe cases I do not undertake to cure; that is, to get them to the point where there will never be a trace of recurrence. I carry the cases to the point of cleaning up the acne and then I let the patient rest, with the idea of continuing the treatment if there is a recurrence. I do that because I think we should be extremely careful to avoid producing changes in the skin in these cases. Some of the deep-seated, indurated acnes that not only last through adolescence but through most of the first half of life cannot be controlled in any other way, and those cases I treat to the point of eradication. I subscribe to the Einstein theory of relativity in regard to the scars. In the badly indurated acne cases there is a destruction of the sebaceous glands of the skin by the roentgen rays, causing more pitting than would otherwise occur, but such patients do not mind a few pits.

DR. HOWARD FOX, New York: There are only two agents which can permanently cure acne, namely, nature and the roentgen rays. In the case of acne of the back we often have to wait many years for nature to effect a cure, and here we must rely on the roentgen rays for the cure of the disease. I have followed the MacKee technic of giving one fourth skin unit, unfiltered, at weekly intervals for a dozen or more weeks. In some patients, particularly blonds, with very delicate skin, I think it wise to lessen the danger of an erythema by increasing the interval between treatments. In such cases there should be an interval of two weeks instead of one after three consecutive treatments. Roentgenotherapy has not cured all of my cases, but I consider it the best method we possess for the treatment of acne. In the hands of an operator who follows the modern measured technic, and who is careful to keep his apparatus, particularly the milliamperemeter, in good working order, this method is not only effective but also safe.

DR. ERNEST L. McEWEN, Chicago: Regarding the question of pitting in acne following the use of the roentgen ray, I can hardly accept the theory that it is merely a relative matter. Cases occur in which the pitting after the use of the roentgen rays is more than one would expect after other forms of treatment. I recall one case of severe acute acne in which there was prompt relief after

treatment with the roentgen rays, in which the pitting was so extensive that the patient for a time was decidedly threatening in her attitude. I think the pitting in pustular acne as a result of roentgen ray treatment is analogous to the scarring which occurs in smallpox in that exposure to actinic rays is known to increase the degree of pitting and scar formation in the latter disease.

DR. L. B. KLINE, New Haven, Conn : There should be no question as to the efficiency of this method in the treatment of acne, but a word of warning should be sounded. We have found cases of reactivation of tuberculous foci in the lungs following roentgenotherapy in the treatment of acne vulgaris. In the question of the raying of facial acne vulgaris, I doubt if it would be more than a slight thing. The great danger would be in the treatment of acne of the chest, where the ray would be placed directly over the process. We have found that even a slight exposure increases the tuberculosis. In following this most excellent treatment for acne vulgaris we should bear in mind that when a patient also has tuberculosis we should be extremely careful in the treatment of such cases. I have seen this reactivation occur in five or six instances. We have modified our treatment a little and are using not only the roentgen ray but actinotherapy and the Kromayer light in combination with roentgenotherapy.

DR. WILLIAM ALLEN PUSEY, Chicago: Since I began working with roentgenotherapy I have been on the lookout for evidence of activation of many things, and particularly of tuberculosis by weak roentgen ray exposures. I am willing to admit that activations do occur, but I wish to make my evidence as strong as I can that in my experience I have not been able to find any activations, although I have had them in mind. In my early experience I treated many cases of tuberculosis of the abdomen with small doses of roentgen rays, and I never saw anything to suggest that I was making the patients worse.

DR. WALTER J. HIGHMAN, New York: I do not think Dr. Kline's facts are conclusive or convincing. In the first place, we know the result of roentgenotherapy in cutaneous lesions of tuberculous origin, and we cannot suppose for a moment that in 100 per cent. of cases of tuberculosis of the chest there could have been an activation of the disease through roentgenotherapy any more than through the other forms of actinotherapy. Why should the roentgen ray be blamed? If there were any scientific foundation for the conclusions reached by Dr. Kline, he would be very circumspect in regard to using the roentgen ray in diagnosing lesions of the chest or anything else. Think of the intensity of the rays used in taking pictures and the activation that would be set up by that procedure, which is several times stronger than that used in treating acne. For that reason I wish to go on record as stating that personally I do not believe the roentgen ray has any deleterious effect on tuberculosis of the chest, whether applied on the chest, on the back or on the face.

DR. I. L. MCGLASSON, San Antonio, Texas: In San Antonio we often have cases of tuberculosis, and these patients frequently have acne, sometimes pronounced cases of indurated acne. I have treated many of these cases but have never had any report of difficulty arising from roentgenotherapy in activating tuberculous lesions in the lungs. Dr. Kline's point is not well taken, nor is it worth while considering, for with a large experience with acne in tuberculous patients no results of the kind described by him have obtained in my work. It would seem that if his position is correct, tuberculosis experts should not use radiography in the diagnosis of that disease.

DR. HENRY H. HAZEN, Washington, D. C.: We have rayed the chests and backs of about sixty patients with acne and have no evidence that any of them have developed pulmonary tuberculosis. As to the possibility of getting pigmentation of the face in the treatment with roentgen rays, the best thing is not to be bound by any hard and fast rule. If you find a patient is becoming pigmented, give a little less treatment the next time. I have not had any permanent pigmentation in my work, although some patients have carried pigment for six months.

THE INFECTIVE ORIGIN OF ANOGENITAL PRURITUS

JAMES MACFARLANE WINFIELD, M.D.

BROOKLYN

The dermatologic textbooks discuss anogenital pruritus under the head of general pruritus and, after eliminating such self-evident causes as pediculosis, dermatitis or the irritation from ascarides, and such speculative causes as urethral vegetations, irritation of the utero-ovarian apparatus or some rectal disease, fall back on the time-worn assertion that the local disturbance is a symptom of a general neurosis.

The purpose of this brief communication is to report the results of a study of fifty cases of anogenital pruritus occurring in my private practice during the past few years. It is hoped that it may help elucidate the little understood etiology and treatment of this condition.

AN ILLUSTRATIVE CASE

In 1910, I had an especially obstinate case under observation. A woman, aged 28, had been troubled with true anogenital pruritus for three years. The attack followed immediately after her recovery from the birth of her first child. She had consulted many physicians and surgeons, and all kinds of remedies had been employed, including surgery and the roentgen ray, but, except for temporary relief, the disease had persisted. When I first saw her, she presented the typical picture of a patient suffering from true pruritus. She was emaciated, and showed evidence of loss of sleep and general nervous exhaustion. The skin of the anus, perineum and vulva was thickened, macerated, white in color, and covered with a sticky exudate; there were numerous fissures and scratch marks. Examination of the affected parts did not reveal any disease that could be considered causative of the condition; there was no vaginal discharge, no hemorrhoids, no fissures, nor any rectal disease discernible.

After trying many of the local and internal remedies without any effect, it occurred to me to make a culture of the exudate. A pure culture of the colon bacillus was obtained, a vaccine was made, and the patient received an injection of five hundred thousand bacilli under the skin of the buttock. Twenty-four hours later she thought that she was better. She had had three hours of uninterrupted sleep the night before, an experience that she had not had for months. Thinking the good effect might be psychic, the vaccine was repeated. After she had received five injections varying in strength from 500,000 to 10,000,000, there was no doubt about the improvement in her condition.

She had been able to sleep through the whole night, her appetite had returned, and she had lost the anxious and weary look. The skin of the affected parts was beginning to appear normal. The vaccines were continued until she had received twelve injections in all. The intervals between injections averaged six days. The first 10,000,000 was followed by a sharp constitutional reaction. The only local treatment was cleansing with a 5 per cent. boric acid solution and dusting with zinc stearate.

OBSERVATIONS OF MURRAY

Almost simultaneously with my practically accidental discovery Dr. Dwight H. Murray, of Syracuse, N. Y., was carrying out a series of observations along the same line. His first report was published in *The Journal of the American Medical Association*.¹ At first he found only the *Streptococcus faecalis*, but later he reports the presence of the colon bacillus. He never made a vaccine from the latter, always using one from the streptococcus. In his last report, read before the Section on Gastro-Enterology and Proctology, at the sixty-ninth annual meeting of the American Medical Association,² he gives the summary of eight years of original research work and concludes that "Pruritus ani is caused by an infection made by one of the streptococci group, or associated with it. This infection may be the primary, secondary or aggravating cause. If it is the secondary or the aggravating cause the primary may already have passed away."

He has carried out this line of treatment in over a hundred cases, and has found the streptococcus in 94 per cent.³ The beneficial results and cures obtained by the vaccine treatment justify the belief in the infective etiology of pruritus of the anus and genitals.

Murray's early communications met with considerable skepticism, but now many proctologists, after personal experience, have accepted his views.

I have carefully reviewed the subject of pruritus in all of the available dermatologic literature of the last decade and I have not been able to find a single reference to the possibility of this type of local pruritus being of infective origin.

A REVIEW OF FIFTY CASES

In reviewing the histories of my fifty cases, I find that a majority of the patients, forty in all, had an infection of the skin covering the

1. Murray, Dwight H.: Pruritus Ani: The probable Cause and an Outline of Treatment, *J. A. M. A.* **67**:1913 (Nov. 24) 1913.

2. Murray, Dwight H.: Etiology and Treatment of Pruritus Ani, *J. A. M. A.* **71**:1449 (Nov. 2) 1918.

3. Murray, Dwight H.: Proctologist, St. Louis, **10**:217 (Dec.) 1916.

affected parts, caused either by the colon bacillus or the *Streptococcus faecalis* or by both together. The history of the young woman cited in the foregoing will suffice to illustrate the condition, and for the sake of brevity the forty cases will be grouped according to the clinical findings. All presented the classical appearance of true pruritus of the anus and genitals. Thirty were male and ten were female. In twenty the symptoms were severe and had lasted from three to five years. The remaining twenty were of moderate severity and had lasted from six months to two years. The males were the more severely affected; in only three did the disease involve the scrotum, but in all the perineum was diseased. Four of the females had involvement of the labia, and in one the disease extended over the mons. None of the women had either vaginal discharge or utero-ovarian disease. No patient showed evidence of any rectal disease except one woman who had a few hemorrhoidal tags. The urine of all was examined several times but sugar was never found.

Two of the males had received roentgen-ray treatment and one had been badly burned, but the pruritus had been relieved for only a short time. One other had been treated surgically, and the itching had returned when the patient had convalesced from the operation.

In all of the forty cases the colon bacillus was obtained from the exudate, and in thirty the *Streptococcus faecalis* was demonstrated. Five of the patients in whom the colon bacillus alone was found were treated with a stock vaccine, and the results were as good as when the autogenous vaccine was used. The number of injections necessary to cause an improvement in the condition averaged about five; permanent relief from itching and improvement in the condition of the skin were usually obtained after the patient had received from twelve to fifteen injections. The number of organisms given in each dose ranged from five hundred thousand to one hundred million. Constitutional reactions occurred in ten cases.

All except six patients have remained well to date. In four of the six the pruritus recurred after three months but improved again when treatment was resumed. In the remaining two the recovery from the itching lasted for a year and then recurred, and it has persisted in a modified degree up to the present time, that is, three months.

The only external treatment used in these cases was cleansing the parts with a mild antiseptic solution and dusting with zinc stearate or zinc oxide powder. The patients were instructed to wash the affected parts with soap and water after each defecation.

In the ten remaining cases of the fifty neither the colon bacillus nor the *Streptococcus faecalis* was found. Two women had a severe pruritus of the vulva involving the anterior portion of the perineum;

both had profuse leukorrheal discharge that had existed for over a year, the itching dating from the beginning of the discharge. This leukorrheal discharge was found to be strongly acid. Local alkali treatment relieved the pruritus, and tonics given internally and gynecologic surgery cured both the discharge and the itching.

The remaining eight patients were all male and the histories of the onset and course of the disease were altogether different from those of the cases in which the colon bacillus or the streptococcus was found. They each stated that the first symptom noticed was a slight irritation in the inguinal region, the skin being red, dry and scaly. After a while the eruption extended back along the scrotum, perineum and anus. At first there was little or no itching but as the disease became more nearly chronic this increased until it became intolerable, especially at night. On inspection the remains of the inguinal eruption was found. The skin over the pruritic areas was thickened, slightly red, and covered with a few thin scales. With the exception of one, an obese subject, the skin was not macerated or covered with an exudate. In nearly all there were fissures and scratch marks, especially on the skin of the scrotum.

Three of the patients had, in addition to the anogenital condition, a number of scaly, seborrheic-like patches over the body.

Cultures were made from the scales and the epidermophyton fungus was found. The proper treatment was applied and a speedy cure obtained.

The differential diagnosis between the pruritus caused by the bacillus or streptococcus and that caused by the fungus is simple. The itching caused by the epidermophyton is secondary to an inguinal dermatitis, the skin is neither white nor macerated, and the irritation extends backward over the genitals along the perineum to the anus. The pruritus caused by the colon bacillus or the streptococcus begins to itch at the anus and progresses forward, and the skin is macerated and whitish in color. In both types the itching may be equally severe, but in the fungus type it is more readily relieved by scratching and does not seem to the patient to be as deep-seated.

If one considers the various remedies that seem to have a good effect in pruritus ani, it will be found that they all have some antiparasitic action, as, for instance, silver nitrate, phenol and the roentgen-ray, and, one might add, the thorough ante-operative cleansing. All this has helped to strengthen the belief that most cases of true anogenital pruritus are of infective origin.

The reason why the roentgen ray, surgery or antiparasitic remedies do not produce a permanent cure is because the resistance and

metabolism of the skin is lowered by some cause, and while anti-pruritics, the roentgen ray, etc., may produce a temporary relief, nothing has been done to raise the resistance of the skin over the affected parts.

SUMMARY

In over 90 per cent. of all cases of true anogenital pruritus, either the colon bacillus or the *Streptococcus faecalis* was found on culture.

In these, 90 per cent. of cures or relief was obtained by treating the patients with a vaccine made from these cultures.

Tineal infection can cause a pruritus of these parts that closely resembles true pruritus.

47 Halsey Street.

Abstracts from Current Literature

A POSSIBLE EXPLANATION OF THE INCREASED INCIDENCE AND EARLY ONSET OF NEUROSYPHILIS. A. REITH FRASER and A. G. B. DUNCAN, *Brit. J. Dermat. & Syph.* **33**:251 (July) 1921.

In this interesting article Fraser and Duncan call attention to the increase of neurosyphilis. They state that since the war there has been a general increase of nonsyphilitic nervous disorders and that it is possible there may be some increase of susceptibility. This does not explain, however, the vast increase of early central nervous system involvement in syphilis since the dawn of the arsphenamin era.

They call attention to the fact that the treatment of syphilis is now often a routine, dominated by pathologic findings and serologic reports, while clinical acumen, the consideration of the individual case and the fundamental aims of chemotherapy are neglected.

They feel that in the present method of treatment the aim appears to be to render the organisms dormant and to allow the patients' resistance to look after itself when required, whereas the real aim of chemotherapy is to stimulate antibody production and to kill the attacking organisms or render them dormant.

In syphilis it is most probable that antibodies are carried to the cerebrospinal fluid axis by the blood stream. Their presence in the cerebrospinal fluid is probably accidental, as also is the presence of spirochetes, as they are found in the spinal fluid because they happen to be present in the meninges or because the choroid plexus has become unduly permeable. Thus the intrathecal supply of antibodies is much weaker and more limited than the supply available in the general systemic circulation, and to a very considerable extent dependent on it. The presence of spirochetes stimulates the mechanism of immunity, and antibodies, whatever their nature, are produced. Arsphenamin is toxic to the spirochetes, and as they are killed the stimulus of antibody production is removed, for arsphenamin does not cause any output of antibodies. Unfortunately the drug does not kill all the organisms as a rule, while both the arsenic and the diamino radicles are toxic, damage the tissues and lessen the power of producing any further supplies of antibody.

The authors then call attention to the fact that arsenic tends to injure the cerebrospinal axis, and that it seems likely that an arsenical spirochetocide may injure the nerve tissues. Thus, if all the spirochetes are not killed, the damaged central nervous system may be the weakest site for attack by the survivors.

The authors then discuss the course of a hypothetical case of syphilis under (a) no treatment, (b) treatment with mercury and iodid, and (c) modern intensive treatment.

The paper, which is to be continued, closes this part with a consideration of the occurrence and clinical signs of early neurosyphilis.

SENEAR, Chicago.

DERMATITIS HERPETIFORMIS. G. W. SEQUEIRA, *Proc. Roy. Soc.* **14**: 81 (July) 1921.

A man, aged 48, who had had dermatitis herpetiformis for eight years and who had had the various usual remedies without improvement, had obtained comparative relief by taking antimony in connection with arsenic.

GUY, Pittsburgh.

CONTRIBUTION TO THE MICROBIOLOGY OF SYPHILIS. ORIGINAL RABBIT SYPHILIS. I. SCHERESCHESWSKY and WERNER WORMS, Dermat. Ztschr. **33**:10, 1921.

Earlier investigators, notably Arzt and Kerl, have reported the occurrence of an original rabbit syphilis, caused by an organism indistinguishable from that of human syphilis. Arzt and Kerl found seventy-two, or 26.9 per cent., of 853 rabbits affected with this disease. The breeders were certain that the animals had never been used for experimentation, nor any other rabbits that they may have come in contact with. Arzt, in 1919, found the same disease six times among nineteen grown animals of a stock of thirty-five. The source of the animals, Innsbruck, had never been previously used for experiments. This author was led to believe that he was dealing with an original rabbit syphilis. After the work of Kolle and Ritz, who reported that they had a strain of syphilis from a human source which had been carried from one rabbit to another by coitus for over twelve years and had made over eighty animal passages, Arzt considered that he may have been dealing with a rabbit syphilis whose ultimate source was human.

Schereschewsky, in the fall of 1919, received an animal, male rabbit No. 516, sent as absolutely normal and investigations later showed that there had been no possibility of experimentation. This animal showed a papule on the buttock from which spirochetes were demonstrated. These spirochetes were absolutely indistinguishable from *Spirochaeta pallida*. New papules made their appearance at the base of the penis, on the glans, and the first lesion persisted. Normal females showed similar lesions and spirochetes after coitus with this male. When rhagades were present, infection was aided as in human syphilis. The use of a glass capillary pipet which acted as an inoculation instrument and reservoir of material made infection certain. The authors, considering themselves fortunate in having a spirochetal genital disease which was sexually transmitted, sought to recapitulate the studies on syphilis. Although having a high virulence for rabbits, these spirochetes were nonpathogenic for white mice, rats, guinea-pigs and a *Cynomolgus* monkey. The infection in rabbits followed an incubation period of from fourteen to twenty-five days. The earliest lesion was of maculopapular form and rich in spirochetes. There was no swelling of the glands. The lesions persisted a long time, and as long as they remained spirochetes were present. Lesions of possible secondary type on the snout and keratitis were not conclusive. The young of mating when either one or the other partner was diseased did not show evidences of syphilis. In one an enlarged spleen and liver gave no spirochetes on examination. Reinfection, superinfection and cross infection with known human spirochetes were all possible, but because of the status of immunity in rabbit syphilis, no conclusions can be drawn. The use of a quinin ointment devised by Schereschewsky and manufactured by Merck was found protective.

GOODMAN, New York.

EPIDERMOLYSIS BULLOSA. H. W. BARBER, Proc. Roy. Soc. **14**:85 (Aug.) 1921.

A boy, aged 9, with a typical epidermolysis bullosa was presented. The chief point of interest in connection with the case was that twenty-two members of the family were similarly affected.

GUY, Pittsburgh.

SALHYRSIN. DR. EISLER, *Ceska dermat.* **1**:80, 1920.

Salhyrsin is a new derivative of arsenic and mercury (3 per cent. salicylate). It comes in 2 c.c. ampules, the daily dose being from 2 to 4 c.c. given intramuscularly.

This new antisyphilitic preparation was tried out on eighty patients in the dermatologic clinic of Prague. There were no local or general reactions following injections. Administration causes little pain. Salhyrsin has only mild antisyphilitic properties, but has an excellent tonic effect on syphilitic patients and makes a valuable preliminary drug to mercurial treatments. Patients who received salhyrsin responded to mercury much more rapidly and stood it well. The article gives the clinical course of patients thus treated.

CEPELKA, Chicago.

THERAPY OF HYDROA AESTIVALIS. CESTMIR PARANA, *Ceska dermat.* **2**:44, 1920.

The eruption was localized on typical places and appeared in the form of erythema and tubercles. The patient gave the history of profuse menses lasting from seven to ten days. During this period she usually felt better. Physical examination revealed incipient tuberculosis. The menstrual history being striking, ovarian extract was prescribed, with a surprising effect. The eruption disappeared in two weeks in spite of sunny days. It returned when the extract was omitted, and disappeared again under its use. The extract, however, had no effect on her menses.

CEPELKA, Chicago.

METHOD FOR REMOVAL OF NATURAL AMBOCEPTOR FROM HUMAN SERUM. R. L. KAHN, *J. Lab. & Clin. Med.* **6**:218 (Jan.) 1921.

The method described by Kahn is based on the well-known affinity of sheep cells for antishoop amboceptor, and consists of adding packed sheep cells to inactivated serum in the proportion of one drop per cubic centimeter of serum, and permitting the extraction to take place for ten minutes at room temperature.

WAUGH, Chicago.

COOLING POWDERS AND SALVES. O. RYBAK, *Ceska Dermat.* **2**:201 and 234, 1921.

The author attempts to ascertain by what mechanism the cooling effect of inert powders and cooling salves is produced. His experiments show that a layer of powder applied to the skin increases the actual evaporating surface by its own volume only two and one-half times at the best, and, therefore, is not sufficient to cause a noticeable effect. Microscopic observations of a perspiring skin show that the droplets of sweat occupy the openings of sweat ducts and that they spread along the papillary ridges, where the evaporation takes place. The fields between the skin markings are normally dry. A layer of powder applied to the skin attracts the sweat and spreads it over the entire skin surface, over areas where evaporation usually does not take place.

The effectiveness of a cooling powder depends on the amount of moisture on the skin; the moister the skin, the greater the cooling effect obtained. The composition of the powder also plays a part. The evaporation from a

saturated zinc oxid layer is more rapid than from a saturated talcum or starch surface. Any indifferent powder can act as a cooling agent if applied in a thin layer. Put on heavily, a cooling powder becomes a drying application.

The effect of cooling salves (classic formulas: lanolin 2 parts, petrolatum 1 part, water 1 part) is produced by the evaporation of water they contain, and is, therefore, effected even on a dry skin, provided the surface be uncovered. An addition of some porous, water-conducting substance, such as starch, will increase the cooling effect of the ointment considerably. Such substances must be added in sufficient amounts (starch 16 per cent. minimum). Talc (non-porous) does not increase the rate of evaporation. The addition of talc to cooling salves is useless. (Zinc oxid, also nonporous, is the usual ingredient of cooling salves for its chemiotherapeutic effect on inflammations and for its preservative effect.) Terra silicea, 1 to 3 per cent., which is very porous and does not decompose, constitutes an ideal ingredient of cooling salves.

SPINKA, St. Louis.

EXTRAGENITAL PRIMARY INFECTIONS DURING THE YEARS OF THE WAR, 1914-1918, WITH SPECIAL CONSIDERATION OF TONSILLAR PRIMARY INFECTIONS. MEYER, *Dermat. Wchschr.* **72**:153 (Feb. 25) 1921.

The author has gained the impression from the admissions into the hospital of St. George at Harburg that there was an appreciable increase in the number of extragenital infections during the years of the war out of proportion to the augmentation of syphilis in general. Extragenital lesions were relatively more frequent in women than in men. Cohabitation by mouth was an infrequent cause of oral syphilis. The infection usually was acquired through kissing, from food utensils or the use of wind instruments.

The paper first describes the common forms of extragenital primary infections and then emphasizes the frequently overlooked tonsillar primary infections. Chancre of the lip is usually characteristic—a small round, slightly raised, flat erosion on the inner half of the mucosa, appreciably firm on palpation and often covered with a crust. Frequently there is a round or oval hard swelling, with raised edges. The center may be crateriform and the floor lardaceous or bloody. There is an indolent swelling of the regional lymph glands. Chancres of the tongue resemble those of the glans penis, as either a slightly raised swelling or with tissue destruction forming a sharply circumscribed swelling with a hard base. Tonsillar primary lesions are often erosions with light, grayish-blue shimmering coatings. These have lacquer-colored edges and may show slight tissue destruction. It is essential to distinguish these lesions from Plaut-Vincent's angina and diphtheria. Tuberculous cervical adenitis and malignant tumors are easily distinguishable from these lesions. Dark-field examination and gland puncture should be done in all suspicious cases. Finger chancres are often overlooked in their early stages and treated by surgical measures until the secondary areola appears.

ANDREWS, New York.

SYPHILIS OF HIDDEN ORIGIN, FIRST MANIFESTED BY LYMPH NODE INVOLVEMENT (SYPHILIS A BOUBON D'EMBLEE). AUDRY and CHATELIER, *Ann. de dermat. et syph.* **7**:304 (July) 1921.

Five cases are reported: (1) an insignificant erosion of the penis, accompanied by a suppurating polyadenitis, whose syphilitic nature was only revealed

by the Wassermann reaction, (2) a typical erosive balanitis accompanied by suppurating polyadenitis and a positive Wassermann reaction, and (3) three cases of suppurating polyadenitis without any appreciable portal of entry, whose nature was ascertained only through the Wassermann reaction.

In the discussion various possibilities are considered, the authors concluding that certain cases of syphilis do not begin with a macroscopic chancre: 1. Some follow a direct inoculation of the blood stream (as in experimental syphilis, the congenital affection, or the introduction of spirochetes by a needle-jab). 2. Spirochetes may be absorbed from a lesion caused by some other infection, not syphilitic. 3. Much more frequently the chancre is microscopic and therefore overlooked. An intense reaction of the satellite lymph nodes seems to be characteristic.

PARKHURST, New York.

CONTRIBUTION TO THE STUDY OF PARAPSORIASIS. L. MARTINOTTI.
Gior. ital. d. mal. ven. **57**:205 (June) 1921.

The author outlines the history of parapsoriasis from the early publications of Unna, Santi and Pollitzer in 1890 on "Parakeratosis Variegata," those of Jadassohn on "Dermatitis Psoriasiformis Nodularis" in 1894, those of Brocq in 1897 on "Erythrodermie Psoriasiforme en plaques disséminées" and the more recent contributions of Colcott Fox, MacLeod, Juliusberg and Crocker. Brocq united under the term "Parapsoriasis" all the different clinical types described, and this denomination has been generally accepted.

The group of parapsoriasis is formed by a number of dermatoses of chronic evolution, characterized by slight subjective symptoms, by the presence of macules or patches of pink to red color with a pityriatic desquamation and the absence of constitutional symptoms. Histologically there is edema of the rete, thinning of the corneus layer and atrophy of the granular layer; in the corium, flattening of the papillae, dilatation of the blood vessels and perivascular infiltration of round cells.

There are three varieties of parapsoriasis according to Brocq: (1) parapsoriasis en gouttes, identical with exanthema lichenoides psoriasiformis (Jadassohn) and pityriasis lichenoides chronica (Juliusberg); (2) parapsoriasis lichenoides, identical with parakeratosis variegata (Unna) and lichen variegatus (Crocker); (3) parapsoriasis en plaques, identical with xanthoerythrodermia perstans (Crocker) and erythrodermie pityriasique en plaques disséminées (Brocq).

The author reports six cases of parapsoriasis of the different types. He criticizes the classification of Brocq and concludes that it does not include all the cases; that there are many intermediate clinical conditions that cannot be placed in any of the three types, and that many cases beginning as a definite clinical variety, may change later in the course of the disease and present a different eruptive form. He thinks with Riecke that it is better to place under the name "Parapsoriasis" or "Paralichen" or "Erythrodermia squamosa, maculosa and papulo-maculosa," the following three types that seem to include all the cases published up to the present: first type, erythrodermie pityriasique en plaques disséminées (Brocq), parapsoriasis en plaques (Brocq), pityriasis maculosa chronica (Rasch), erythrodermia maculosa perstans chronica (Riecke), erythro-atrophodermia perstans en plaques (Pernet), erythrodermia maculosquamosa perstans (Galloway), erythrodermia squamosum (Ravogli), xantho-erythrodermia perstans (Crocker). This type might be called "Brocq's Disease." Second type, dermatitis psoriasiformis nodularis

(Jadassohn), exanthema psoriasiformis lichenoides (Neisser), pityriasis lichenoides chronica (Juliusberg). This type might be called "Jadassohn's Disease." Third type, parakeratosis variegata (Unna, Santi and Pollitzer), lichen variegatus (Crocker). This type might be called "Unna-Santi-Pollitzer's Disease."

The article is illustrated with fourteen clinical photographs and four photomicrographs. The bibliography is extensive.

PARDO-CASTELLO, Havana.

CLINICAL LECTURES ON DERMATOLOGY. ECZEMA AND DERMATITIS. P. G. UNNA, *Dermat. Wchnschr.* **72**:233 (March 26) 1921.

Eczema was originally an expression for furunculosis among the Greeks. This usage persisted to modern times until Willan (1789-1808) separated a small, concise group of dermatoses, characterized by densely grouped, numberless small vesicles on an inflamed surface, etiologically distinguished because acutely produced by certain irritants like turpentine or sunlight, which disappeared with the removal of the irritant. To this group Willan transferred the ancient name eczema.

This nomenclature was adopted in Paris by Rayer. A remarkable misunderstanding occurred in these prebacterial times, probably due to Rayer's unfamiliarity with English. He understood Willan's vesicular eczema as the acute beginning of an altogether different chronic skin disease, which Willan had placed in his group of impetigo and prurigo. This formed a chronic polymorphous disease in which vesicles were less frequent than scales and crusts. This present conception of eczema must be separated from the artificially created vesicular dermatitis of Willan. The eruptions grouped by Willan under the name eczema have nothing to do with Rayer's eczema, but may occasionally appear on eczematous surfaces after the use of irritating applications. Eczema may appear during the course of a dermatitis due to the entrance of eczema organisms through the injured epidermis. Such antecedent dermatoses are important in the correct conception of many face, hand and occupational eczemas and for their therapy.

ANDREWS, New York.

DOSAGE MEASUREMENT. CORRESPONDENCE. JOHN REMER and WILLIAM D. WITHERBEE, *Am. J. Roentgenol.* **8**:417, 1921.

In reply to Shearer's criticism, the writers wish to state that their formulas and methods of determination of roentgen-ray dosage were based on Holzknecht radiometer readings and clinical manifestations on the human skin, also on nearly four years of actual operation in both clinical and private practice with standard apparatus. Their modification of the radiographic formula $\frac{MA \times V \times T}{D \times D}$ was determined by a series of readings in which they found that doubling the spark gap without changing the other factors gave double the dose as indicated by the radiometer scale. This was clinically verified. They therefore adopted the following formula for unfiltered therapy: $\frac{MA \times SpGp \times T}{D \times D}$. They also found that when a filter of aluminum was interposed, it only required twice the time to produce the same Holzknecht reading at full distance as that at half distance. This was also verified by clinical experiment. It seemed then that determinations of filtered roentgen-ray dosage based on the same law of distance as in unfiltered dosage would involve disregarding

entirely the clinical manifestations of the skin and would ultimately lead to permanent disfigurement, telangiectasis, keratosis and epitheliomatous degeneration of the exposed skin. Unless some method is devised whereby the law of light and distance and the clinical manifestations of the human skin in filtered therapy coincide, the writers can see no reason why a law of physics should form the sole basis of determining dosage.

GOODMAN, New York.

X-RAY TREATMENT OF SKIN TUBERCULOSIS. K. GAWALOWSKI.
Ceska Dermat. 2:225.

This paper, written for the Scientific Society for the Fight Against Tuberculosis, reviews and discusses the theories regarding the biologic effect of roentgen rays on the pathologic tissues, particularly the tuberculous. The author arrives at the conclusion that the view maintaining that healing in skin tuberculosis under irradiation is effected by an increase in the cellular formation of antibodies is as well substantiated as the theory of disintegration of pathologic tissue and overgrowth of normal connective tissue. Neither view, however, explains the resistance to irradiation of lupus vulgaris involuted to the stage of lupus planus.

Discussing the dosage used in the treatment of skin tuberculosis, the author compares the varied technics used by the different authorities. It is certain that a superficial epilating dose is strong enough to destroy the tubercle. Meyer alone uses the full epilating dose, others favor half the strength or slightly more. As the question of cellular immunity in tuberculosis is not definitely settled and it is not known yet which cells form the antibodies in tuberculosis, it is important to avoid doses that would decrease the vitality of the skin. At the Clinic of Prague with its comparatively limited facilities for a large number of patients, roentgen-ray treatments are in many cases combined with phototherapy. Finsen treatment is used on almost all face cases. The author reports good results in affections of the mucous membranes. To save time he uses small doses and thinner filters.

SPINKA, St. Louis.

ON THE RAVAGE OF CONGENITAL SYPHILIS AND ITS PREVENTION. S. HATA, Internat. J. Pub. Health 2:354 (July-August) 1921.

Hata noted that 40 per cent. of married women who had positive blood Wassermann reactions were sterile, while 60 per cent. had been impregnated. In all instances, the women had been married for three years or longer. He thinks that the percentage of sterility would be higher if all married women were subjected to the Wassermann test.

The following suggestions are offered for dealing with the prevention of congenital syphilis:

"1. To institute a propaganda pointing out the personal and social ravages of congenital syphilis and also the possibility of transmission of syphilis by women showing a positive Wassermann who may be quite unaware of having syphilis.

"2. To disseminate, more strenuously, information about congenital syphilis among midwives and to teach them that if there is the least apprehension of syphilis in a pregnant woman or her husband, or if a pregnant woman has previously given birth to a premature fetus, they should advise her to undergo the blood test.

"3. If a pregnant woman should show a positive Wassermann, she should be given antisyphilitic treatment without loss of time, should her environment permit.

"4. The new-born baby of a syphilitic woman should have its blood examined and, if a positive Wassermann is found, proper antisyphilitic treatment should be given and the baby put under long continued observation.

"5. If either one of a married couple should have syphilis the other's blood should also be examined."

In addition, public opinion should be molded so that all engaged women would submit to a Wassermann test.

MICHAEL, Houston, Texas.

PSORIASIS PUSTULOSA. ROBERT SCHAEFER, *Dermat. Ztschr.* **33**:49, 1921.

Schaefer adds a third case to those reported by V. Zumbusch and Koenigsbeck. Although abscesses are recognized in the histologic study of psoriasis, it is rare indeed to have pustules appear macroscopically. Schaefer's patient had the disease for ten years. There was recurrence of grouped pustules, which became confluent, and after bursting left a crust. When this was removed, scales were present and on manipulation minute bleeding points were visible. The pustular process was superficially in the epidermis, and there was an associated parakeratosis and hyperkeratosis. The diagnosis of pustular psoriasis was made. Later the patient returned with lesions of ordinary psoriasis for the first time while under observation.

GOODMAN, New York.

CONTRIBUTION TO THE STUDY OF THE ETIOLOGY OF IMPETIGO HERPETIFORMIS. J. CAPPELLI, *Gior. ital. d. mal. ven.* **57**:187 (June) 1921.

The author reports a case of impetigo herpetiformis in a pregnant woman. The disease appeared in the sixth month of pregnancy in the form of a pustular eruption involving the axillae, the chest, the groins and the adjacent parts of the thighs. Some dark, moist, vegetating lesions could be seen in the axillary folds, resembling the lesions of acanthosis nigricans. Fever and considerable general disturbance were present. During the seventh month the patient gave birth to an apparently normal child, who died shortly after. Four months later the patient was discharged from the hospital as cured. After two years she became pregnant again, and the eruption appeared during the sixth month of pregnancy as before, with a high temperature and considerable general derangement. During the seventh month, after a premature childbirth, the patient began to improve and was soon discharged in good condition. Numerous examinations made by the author have led him to believe that impetigo herpetiformis is a well defined clinical entity, entirely different from herpes gestationis and dermatitis herpetiformis of Duhring. *Staphylococcus pyogenes aureus* was recovered in pure cultures from the lesions. Biologic tests showed the existence of increased thyroid and suprarenal secretions. He concludes that the disease is caused by an infectious and toxic agent due to or closely connected with pregnancy.

PARDO-CASTELLO, Havana.

CLINICAL LECTURES ON DERMATOLOGY. EPIDERMATITIS. P. G. UNNA, *Dermat. Wchnschr.* **72**:217 (March 19) 1921.

The conception of inflammation dates back to ancient history and resolves itself into a complex of the four related symptoms: redness, heat, swelling

and pain. The fundamental idea of an epidermatitis, however, is still uncertain among physicians. The symptoms are redness, vesiculation and crust formation.

The inadequate theory of Cohnheim that inflammation consists of a sudden increased permeability of the blood vessel walls, a dilatation of the vessels and a slowing of the blood stream with a migration of leukocytes into the neighboring tissues, is but vaguely applicable to epidermatitis, of which impetigo of Bockhart is an example. The picture is a drop of pus evolving with uncanny suddenness between the horny and prickle cell layers far distant from blood vessels.

Chemotaxis, discovered by Pfeffer and elaborated by Leber, explains distant effects on the basis of chemical affinity between the irritant and the vessel contents. The slowing of the blood stream, congestion and dilatation of vessels is secondary to this externally applied force. The stream of "wandering" leukocytes has a definite direction and limited scope. Inflammation of the epidermis was first favorably explained by chemotaxis. This applies also to avascular parts, such as the follicles, sebaceous and coil glands.

Inflammations of the derma and subcutis, as exemplified by erysipelas, may depend for explanation on either or both of these doctrines.

ANDREWS, New York.

ECZEMA IN THE BREAST-FED BABY AND PROTEIN SENSITIZATION. E. S. O'KEEFE, Boston M. & S. J. **185**:194 (Aug. 18) 1921.

O'Keefe reports forty-one consecutive cases of infantile eczema, which were exclusively breast fed. These cases were treated in a subclinic of the Children's Medical Department of the Massachusetts General Hospital in conjunction with local treatment given by the dermatologic department. Skin tests were made on all cases and 61 per cent. showed positive reaction to one or more proteins used. Forty-one per cent. showed positive reaction to egg protein, and 39 per cent. to cow's milk protein. No sensitized case failed to show a positive response to either egg or milk protein.

He suggests that sensitization has occurred, apparently through foreign proteins ingested in the breast milk.

There was apparent cure in about 40 per cent. of these cases, and definite improvement in about 20 per cent. more of the cases has followed the omission or limitation in the maternal diet of one or more food proteins to which the infant is sensitive.

LANE, Boston.

PATHOGENESIS OF LIVEDO RACEMOSA AND ALLIED CONDITIONS. L. HESS and W. KERL, *Dermat. Ztschr.* **33**:125, 1921.

The authors review the condition of cutis mammorata and add the disease described by Ehrmann and designated as livedo racemosa. The latter condition is not ordinary livedo because it has the coloration reversed; the spots are livid and the surroundings white, and the spots are not influenced by treatment or by warmth. They have seen eight examples of this disease. Abnormalities of internal organs could be demonstrated in each of the patients, but no abnormality was constant. The patients were of the nervous type, with skin, even in the male patients, that reminded one of the female skin. Histologic

studies in four cases failed to reveal any abnormality of the vessels, either arteries or veins, nor any infiltration of sufficient mass to hinder the circulation. No etiologic factor could be determined by the histology.

GOODMAN, New York.

SOME REMARKS ON THE DIAGNOSIS AND TREATMENT OF CONGENITAL SYPHILIS. MARSHALL, *Brit. J. Child. Dis.* **208-210**: 57 (April-June) 1921.

The author sees an apparent increase in visceral and nervous syphilis. He considers as the most important early diagnostic signs: desquamative eruptions on the palms and soles, enlargement of the liver and spleen, epiphysitis, fissures about the mouth and orchitis.

Among the many alleged dental manifestations of syphilis, Hutchinson's notching is said to be the only absolutely diagnostic sign. Interstitial keratitis is mentioned, its prognosis depending on the presence or absence of concomitant choroiditis. The characteristic syphilitic deafness, due to hyperplastic labyrinthitis, is usually bilateral. Considering syphilis of the bones, the author mentions epiphysitis and the resultant "syphilitic pseudo-paralysis," also dactylitis, with points of differentiation from the tuberculous form. He lays great stress on the value of the therapeutic test in diagnosing bone syphilis. The presence of syphilis paves the way for tuberculosis. In visceral syphilis, so often difficult to diagnose, Marshall recommends the therapeutic test. He considers the effect of the disease on the endocrine glands, and by way of treatment he advises the combination of opotherapy with the usual arsphenamin and mercury. The involvement of the nervous system is discussed, and finally the matter of acquired syphilis in children.

Treatment, antenatal and postnatal, is outlined. The author prefers the method of intramuscular administration in giving arsenicals. After thorough treatment, the persistence of a positive Wassermann reaction should cause no alarm.

PARKHURST, New York.

QUANTITATIVE ESTIMATION OF THE TOTAL PROTEIN IN THE CEREBROSPINAL FLUID. J. B. AYER and H. E. FOSTER, *J. A. M. A.* **77**:365 (July 30) 1921.

Realizing the value of quantitative protein estimations of the cerebrospinal fluid, the authors sought the aid of Dr. Denis, who devised a colorimetric method which they have used to determine the protein content in various diseases of the central nervous system. (A preliminary report giving the technic of the method was published in *Arch. Int. Med.* **36**:436 [Oct.] 1920.) They believe that any total protein quantitation above 40 mg. per hundred cubic centimeters is pathologic.

In studying cerebrospinal fluid of patients under treatment for neurosyphilis, it was noted that protein begins to fall early in all forms except paresis; in the latter it may even increase, although the cell count is dropping.

They give a table with appended comments of their findings in various diseases of the cerebrospinal system. Total protein estimation is of particular value because it gives results in more certain and intelligent form, renders more significant slighter degrees of abnormality and thus makes diagnosis more acute.

MICHAEL, Houston, Texas.

EXPERIMENTAL INVESTIGATION CONCERNING THE MOVEMENT OF SKIN PIGMENT. HEINZ MEYER, *Dermat. Ztschr.* **32**:348 (April) 1921.

Several factors are probably at work in regulating the epidermal pigment. The greatest portion of the pigment is carried off by the horny layer, which in hundreds of sections studied was seen to be carrying off great masses of pigment as the layer is lifted off. The second route for passage of the pigment from the epidermis is by way of the lymphatics. Evidence cannot be brought forth in as much volume for this way as for the other because of the technical difficulties in section cutting. The glands are filled with pigment. Since no thought has been advanced that the nodes prepare pigment this must have been brought to the nodes. One cannot be certain that the cells of the cutis have any part in forming pigment. The numbers of cells from the cutis laden with pigment is very small, and in many preparations no such cells were found. Such cells may also be carriers of pigment and not formers of it. The question could not be decided by the investigations of the author.

GOODMAN, New York.

METABOLISM IN PELLAGRA: A STUDY OF THE URINE. M. X. SULLIVAN, R. E. STANTON and P. R. DAWSON, *Arch. Int. Med.* **27**:387 (April) 1921.

The results of these investigations at the United States Pellagra Hospital are as follows: Mineral metabolism was abnormal, especially in the active state although the diet was abundant. An increased putrefaction in the intestines was noted, and about 50 per cent. of the patients showed kidney change by the presence of albumin and casts, although such a change may not occur even in marked cases.

A low total nitrogen and ordinary urinary ingredients were found, as well as a low urea which occurred even in some cases in which the total amount of nitrogen was fair.

Ammonia nitrogen and undetermined nitrogen were increased; uric acid and creatinin were low, while the utilization of protein was subnormal.

After at least a month of curative diet, the urinary ingredients gradually approached normal, and the writers agree that there are at least two types of pellagra: (1) that in which marked skin symptoms and little physical degeneration occur and (2) that exhibiting the reverse. The latter type showed greater abnormalities in urinary findings.

JAMIESON, Detroit.

CARCINOMA CUTIS IN ANTHRACENE WORKERS. W. J. O'DONOVAN, *Proc. Roy. Soc.* **14**:73 (June) 1921.

A man, aged 62, who for three years had been working unloading sacks of anthracene cake developed an irregular, circular, raised, flat tumor with over-hanging edges and an ulcerated granular, slightly scabbed surface, on the back of his right wrist. The growth was of six months' duration. It began as a small black topped wart which was repeatedly injured by bumping against the top of a tub. Microscopically the lesion was a squamous-cell carcinoma. Anthracene cake is a green moist amorphous powder containing 40 per cent. of anthracene ($C_{14}H_{10}$) and smelling strongly of cresols. Anthracene is one of the higher boiling portions of the distillate from coal tar. Three similar cases, which are reportable, had been seen during the past year.

Guy, Pittsburgh.

SCLERODERMA IN BANDS WITH MULTIPLE PIGMENTED SPOTS.

G. THIBIERGE and RABUT, Bull. Soc. franç. de dermat. et syph. **5**:174, 1921.

In 1914, after a nervous shock, a girl of 10 years noticed the appearance of brownish spots in her skin, which soon faded, only to reappear after another shock in 1917. These spots had persisted, involving the left side of the neck, the dorsolumbar part of the back and each flank. The patch on the neck consisted of numerous pale, thickened macules on a deeply brownish base; the lesions of the back and flanks showed no thickening, but they were pigmented.

Unlike most scleroderma plaques, these were sharply circumscribed. Unlike the usual scleroderma in bands, the patch in the lower dorsal region was asymmetrical, with no metameric distribution.

PARKHURST, New York.

CONTRIBUTION TO ANATOMY AND BIOLOGY OF THE SKIN.

FURTHER STUDY OF RONGALIT WHITE STAINS OF SKIN NERVES. WALTER FRIEBOES, Dermat. Ztschr. **32**:267 (April) 1921.

In a former contribution, Frieboes commented on the technical considerations of his study. The question is whether the nerve endings are free in the intercellular spaces or not, or whether they are enclosed in an accompanying investing membrane. He investigated the cornea, and several photomicrographs are published which show the nerve endings enclosed. From all his investigations Frieboes concludes that all nerves, even the finest, are surrounded by protoplasmic membranes.

GOODMAN, New York.

ULCEROVEGETATING ANAL TUBERCULOSIS. G. THIBIERGE and RABUT,

Bull. Soc. franç. de dermat. et syph. **5**:173, 1921.

A woman, aged 26, with a negative history, had had anal ulcerations for seven months. On examination there was found an ulcerating, verrucous, typically tuberculous patch, 9 or 10 cm. long and 4 or 5 cm. in width, extending nearly to the vulva. Digital examination showed that the lower 3 or 4 cm. of the rectal wall was also involved. There was no sign of intestinal tuberculosis, but the right pulmonary apex was affected, so that the anal lesion was not considered primary.

The patient also presented a pigmentary syphilid of the neck, and her Wassermann reaction was positive.

PARKHURST, New York.

SOME REMARKS ON THE DEVELOPMENT OF THE LEISHMAN-DONOVAN BODIES. J. E. R. McDONAGH, Brit. J. Dermat. & Syph.

33:182 (May) 1921.

McDonagh, investigating the parasites in several cases of Aleppo button, finds certain variations in the Leishman-Donovan bodies which lead him to believe that he has found an asexual cycle of a coccidial protozoon. If his surmise is correct, he feels that the Leishman-Donovan bodies can be described as the adult or mature form of an asexually reproduced protozoon, which could suitably be called *Leukocytozoon leishmania*.

SENEAR, Chicago.

ULCERATING EPITHELIOMA OF THE BREAST IN A MAN, WITH DERMOHYPODERMIC NODULES IN ITS VICINITY. G. THIBIERGE

and HUFNAGEL, Bull. Soc. franç. de dermat. et syph. **5**:171, 1921.

A glandular carcinoma of the left breast, in a man of 50 years, at first treated as syphilitic, had become extensive, involving the entire breast. A biopsy confirmed the diagnosis too late for surgical aid. These lesions, so unusual in men, are said to be very malignant when attacking this sex.

PARKHURST, New York.

LICHEN SPINULOSUS WITH FOLLICULITIS DECALVANS. E. G. GRAHAM LITTLE, *Proc. Roy. Soc.* **14**:67 (June) 1921.

A woman who had been under observation by different members of the section for several years presented an atrophic folliculitis of the scalp and a typical eruption of lichen spinulosus, the latter being particularly well marked as an exaggerated keratotic mass on the skin behind the right ear. The patient also had lesions on the tongue and buccal mucosa, which were variously diagnosed as leukoplakia and lichen planus. Dr. Little thought that lichen planus might be the explanation of all three conditions.

Guy, Pittsburgh.

ULCERATING LUPUS TREATED BY BENZYL-CINNAMIC ETHER (JACOBSON). A. TZANCK, *Bull. Soc. franç. de dermat. et syph.* **5**:170, 1921.

This remedy, used in pulmonary tuberculosis, was administered to a young man with a stubborn tuberculous ulceration of the hand of sixteen years' duration. After fifteen daily injections of 2 c.c. each, an oily suspension being used, there was immediate marked improvement in the appearance of the lesion, and the hand could be exercised with greater ease.

PARKHURST, New York.

A NOTE ON THE BEST METHOD OF OBTAINING PRECIPITATING ANTISERA. W. D. SUTHERLAND and RAI G. C. MITRA BAHEADUR, *Indian J. M. Res.* **7**:669 (April) 1920.

Sutherland and Baheadur come to the conclusion that the two-dose method of producing antisera gives practically the same result as the three-dose method. They have discontinued the use of intraperitoneal injections, using the intravenous route alone, which they believe to be more efficacious.

GUTIERREZ, Manila.

MELANO-EPITHELIOMA OF THE PALATE. G. B. NEW and F. K. HANSEL, *J. A. M. A.* **77**:19 (July 2) 1921.

The authors give a general survey of the subject and report a case. In a thorough review of the literature they have been able to collect only twenty-four cases of primary melano-epithelioma of the palate.

Their patient, a farmer, aged 62, presented a pedunculated tumor arising from the posterior margin of the hard palate. It was mottled with bluish-green, pink, and black areas, and was very vascular, bleeding easily on manipulation. Clinical and microscopic examination showed it to be a primary melano-epithelioma.

It was treated by thorough cauterization followed by radium and roentgen-ray applications to the site of growth and to the neighboring lymphatics.

When seen some fifteen months later, the growth was still active and nearby lymphatics were involved.

MICHAEL, Houston, Texas.

SYPHILIS OF THE TRACHEA AND BRONCHI. P. M. STIMSON, *Am. J. Med. Sc.* **161**:740 (May) 1921.

Symptoms of involvement of the trachea and bronchi are given as cough with dyspnea or sometimes a small amount of sputum or hemorrhage. A Wassermann test or bronchoscopic examination may be necessary for diagnosis. A report of three cases is given.

JAMIESON, Detroit.

A CASE OF DERMATITIS PALPEBRALIS LICHENOIDES. F. YANG, *Deutsch. med. Wchnschr.* **47**:652 (June) 1921.

The author believes that the disease is due to autointoxication from the bowels. No improvement was seen in spite of every possible therapeutic measure.

AHLSWEDE, Hamburg.

FIXED LUPUS ERYTHEMATOSUS OF THE ENTIRE FACE, SCALP, FOREARMS, HANDS AND THIGH. J. ROEDERER and A. LIX, *Bull. Soc. franç. de dermat. et syph.* **4**: R. S. 23, 1921.

A woman of 26 years, previously well, first noticed the lesions on her face and thigh in 1916, and two years later, when she became pregnant, it spread and involved the scalp, forearms and hands. The lesions had persisted, and were typical of lupus erythematosus, showing some atrophy. Under the influence of various local applications they were disappearing.

PARKHURST, New York.

SYRINGOCYSTOMA. PAUTRIER, *Bull. Soc. franç. de dermat. et syph.* **4**: R. S. 27, 1921.

A man of 34 years, under treatment for pyloric gumma, presented many of these little cutaneous tumors extending over the entire chest. Their appearance was typical, both macroscopically and histologically. They are considered congenital sudoriparous malformations.

PARKHURST, New York.

CHOLESTEROL IN CEREBROSPINAL FLUID. A. LEVINSON, L. L. LANDENBERGER and K. M. HOWELL, *Am. J. M. Sc.* **161**:561 (April) 1921.

Spinal fluids which were positive to the Wassermann and Lange reactions contained no cholesterol in appreciable amounts, and the same is true of normal fluid, which is cholesterol-free or contains a very small trace. Other pathologic conditions, however, such as hemorrhage of the brain, brain tumor, brain abscess and meningitis, showed quantities of cholesterol varying from a trace to a high content. They believe the cholesterol content depends wholly or partially on the permeability of the meninges.

JAMIESON, Detroit.

EPILEPSY AND LATE HEREDITARY SYPHILIS. R. ORTEGA, *Prensa med. Argentina* **7**:258 (March) 1921.

Syphilis may be the direct cause of epilepsy, as pointed out long ago by Fournier. Ortega reports two cases of true epilepsy cured by specific therapy (mercury and neo-arsphenamin). In both cases the Wassermann test was

negative. In the first case the patient had epileptic fits every five or eight days; after eight injections of arsphenamin he was entirely cured, and the attacks have not returned. The author thinks that many cases of epilepsy should be treated as syphilitic, regardless of the Wassermann reaction, although he admits that not all cases of epilepsy are due to syphilis.

PARDO-CASTELLO, Havana.

SYMMETRICAL ASPHYXIAL EDEMA OF THE LEGS IN YOUNG WOMEN THE SUBJECTS OF LYMPHATISM. G. THIBIERGE and J. STIASSNIE. *Bull. Soc. franç. de dermat. et syph.* **3**:67, 1921.

This condition was presented by a young woman, 25 years of age, its duration being about twelve months. From the feet to the middle third of the legs the skin was a violaceous red, and a sharply margined, evenly tumefied area extended upward from the ankles, gradually diminishing in thickness. Palpation conveyed the sensation of edema, but there was no pitting. There was a sort of keratosis pilaris of the legs and thighs, with brownish perifollicular discoloration.

The patient presented a mild hyperthyroidism, with tremor and excitability, but the physical examination was otherwise negative. An injection of tuberculin was followed by a rise in temperature and a marked local reaction, but there was no change in the tumefied areas.

During the past twenty-five years Thibierge has seen several such cases, and he has considered them probably to be allied with the old group of "scrofulous" manifestations, but not identical with Bazin's disease. The rôle of possible thyroid dystrophies in their causation has yet to be proved.

PARKHURST, New York.

ACTINIC RAYS. T. HOWARD PLANK.

This is a discussion of the uses of the ultraviolet ray.

H. R. FOERSTER, Milwaukee.

LUMBAR PUNCTURE. J. KYRLE, *Wien. klin. Wchnschr.* **34**:172, 1921.

Kyrle reviews briefly the history of lumbar puncture and its importance in medicine. As a diagnostic procedure it has become indispensable to the correct interpretation of syphilitic infection in man, and every patient should be punctured, at least for diagnostic laboratory procedures, some time during the secondary course of the disease, the earlier the better for prognosis following proper treatment. Not every case, according to Kyrle, which shows fluid changes, necessarily means ultimate tabes or paresis, even without treatment, because some revert to normal by unaided tissue reactions. Kyrle dilates on the fact that no matter what period it is that the nerve symptoms manifest themselves, it was during the secondary period that the changes were first initiated.

GOODMAN, New York.

SPLENIC ENLARGEMENT OF SYPHILITIC ORIGIN. L. QUEYRAT, *Bull. Soc. franç. de dermat. et syph.* **2**:29, 1921.

A woman, aged 51 years, was found to have a greatly enlarged spleen, firm and smooth on palpation. The blood picture was normal, and a diagnosis of syphilitic splenitis was made by exclusion, the Wassermann reaction being

strongly positive. Potassium iodid was administered in increasing doses, and mercury rubs were given in a short course, succeeded by a number of mercurial oil injections (gray); a month later arsphenamin was given intramuscularly in an oily medium, and several intravenous injections of arsphenamin completed the course. There was a marked decrease in the splenic tumor, but the Wassermann reaction continued to be positive. Goubeau has found syphilitic splenomegaly less rare among children with the congenital infection; mercurial treatment was effective in his cases.

PARKHURST, New York.

PITYRIASIS ROSEA AND ITS RELATION TO TUBERCULOSIS.

R. EISELT, *Ceska dermat.* 1:123, 1920.

The occurrence of pityriasis rosea among tuberculous patients is relatively infrequent. Its appearance has a bad prognostic significance. French authors consider pityriasis rosea a systemic disease related to arthritic and gastric disturbances, while the Germans consider it as a trichophytia. Damary and others believe that pityriasis rosea is the result of bacterial intoxication, that is, with the toxins of tubercle bacilli.

The author describes two patients with pityriasis rosea with manifest tuberculosis but in good general condition, in whom the tuberculosis assumed a malignant character after the appearance of the eruption and ended fatally.

Damary considers the appearance of pityriasis rosea after injection of tuberculin as a reaction analogous to the Herxheimer reaction in syphilis.

CEPELKA, Chicago.

BROMODERMA AND CALCIUM THERAPY. KAREL HÜBSCHMANN,

Ceska dermat. 2:86, 1921.

The author advocates the use of calcium salts in the treatment of bromoderma. The good results are based on the anti-inflammatory properties of calcium; it increases the impermeability of cells and thus directly antagonizes the action of bromin. This clinical observation is well in accord with the results of pharmacologic experiments, and with the present knowledge of colloids and physical chemistry of cells and tissues.

The author cites a severe case of bromoderma in an epileptic girl. She left the hospital completely cured in four weeks. She was given:

	Gm. or c.c.
R Calcium chlorid	50
Distilled water	ad 250

The patient was given one tablespoonful of the solution one hour before meals, three times daily. When well tolerated the dose was increased to six tablespoonfuls daily. Locally the same solution was used in form of compresses on the excoriated lesions.

CEPELKA, Chicago.

TWO CASES OF MICROSPORIA CAUSED BY MICROSPORON AUDOUINI. BOHUMIR REJSEK, *Ceska dermat.* 2:71, 1920.

The author reports two cases of microsporia caused by *Microsporon audouini*, because of their rarity in Central Europe, and because an epidemic did not follow their appearance.

One of the patients developed a number of pustules with considerable induration under treatment, a condition corresponding to the description of kerion celsi. Kerion celsi, according to most authors, never appears in cases of microsporia. If it does, it is usually the result of secondary infection, especially in cases of irritant treatment. In this case the infection started in the area scraped for microscopic specimens, and which the patient did not treat for fear of smarting. Further course of treatment was satisfactory.

CEPELKA, Chicago.

UNUSUAL LOCALIZATION OF PIGMENTARY SYPHILIDS IN LARGE PLAQUES. GRAVAGNA, *Ann. de dermat. et syph.* **3**:121, 1921.

A young man had contracted syphilis eight months previously, with a genital chancre followed by a cutaneous eruption. Thirty injections of mercury biniodid dispelled the lesions, so that the patient did not seek further treatment. Four months after this cessation of treatment the patient noticed the rapid development of smooth dark brown patches on the dorsa of his hands. The patches covered the entire radial side of the right hand and the whole ulnar half of the left. All other causes than syphilis could be ruled out, and when the plaques disappeared three weeks after the institution of mercurial treatment, the diagnosis was firmly established.

PARKHURST, New York.

TWO CASES OF ACNE WITH RATHER UNUSUAL ETIOLOGY.

K. HÜBSCHMANN, *Ceska dermat.* **1**:128, 1920.

The relation of acne to digestive disturbances is well established. Constipation especially plays an important part. It is well known, however, that regulation of diet and catharsis have little influence on most cases. It is necessary to eliminate the cause of constipation.

Case 1 illustrates the clinical course and effect of treatment on a severe case of acne indurata, and a definite improvement from the time when gastric hypo-acidity was diagnosed and regulated. The stools also became normal. Case 2 is one of marked acne vulgaris responding promptly to treatment after dental caries had been remedied.

CEPELKA, Chicago.

LUPUS OF CHEEK OF TWELVE YEARS' DURATION: CICATRIZATION FOLLOWING ONE TREATMENT BY ELECTRO-COAGULATION. P. RAVAUT, *Bull. soc. franç. de dermat. et syph.* **2**:44, 1921.

A girl, aged 18 years, presented a lesion measuring 8 by 12 cm., which was extending in spite of the usual methods of treatment, including a surgical operation. The Heitz-Boyer high frequency apparatus was employed for electro-coagulation with the patient under a general anesthetic. There had been no recurrence of the lupus.

The difficulties and results of phototherapy are discussed, with special reference to the Finsen light.

PARKHURST, New York.

ICEWATER BATH IN COMPLEMENT FIXATION FOR WASSERMANN REACTION. W. W. DUKE, *J. Lab. & Clin. Med.* **6**:392.

The author gives a detailed description of his experiments and concludes that the use of an icewater bath for one hour for complement fixation for

the Wassermann test gives as complete a degree of complement fixation as incubation in the icebox for four hours. The use of an icewater bath, therefore, shortens the refrigeration technic three hours without altering its accuracy. For this reason its use is recommended.

WAUGH, Chicago.

TWO CASES OF REBELLIOUS PRURIGO CURED BY AUTOHEMOTHERAPY. J. NICOLAS, J. GATE and D. DUPASQUIER, *Ann. de dermat. et syph.* **3**:127, 1921.

A severe prurigo associated with tabs in a man of 39 years slowly responded to injections of the patient's own blood, the intervals being five or six days. Five injections sufficed. A man, 59 years of age, presented a prurigo ferex diathesique which was cured by ten injections. Both cases had failed to respond to other methods of treatment.

It is interesting to note that these cases of apparently different origin were cured by the same method of treatment. This therapy should be considered in any resistant prurigo.

PARKHURST, New York.

CASE OF UNUSUAL SUSCEPTIBILITY TO IODIN. H. E. HAPPEL, *J. A. M. A.* **76**:1164 (April 23) 1921.

In the course of a supravaginal hysterectomy a small quantity, less than a drop, of tincture of iodine was applied to the cervical stump. Seventeen hours later, the patient began to complain of an intense itching and burning of the skin, followed by the appearance of typical wheals. The attack lasted two days, temporarily relieved on two occasions by epinephrin injections. Nine years previously, the patient had a similar experience following the application of iodine to the skin of the neck.

MICHAEL, Houston, Texas.

WHY IS LEPROSY NOT YET EXTINCT IN NORWAY? H. P. LIE, *Acta dermat.-ven.* **3-4**:297 (Dec.) 1920.

The official number of lepers in Norway has steadily decreased from 2,858, in the year 1856, to 180 in 1919. The author gives the history of six recent cases to illustrate the inability of the average practitioner to diagnose the disease, and also to show the lack of hygienic supervision toward preventing contagion. The fault lies with the medical schools, and if conditions are to be improved, patients must be kept in the teaching centers where they can be seen and examined by students. With early diagnoses and proper care, chances of contagion will be diminished and the disease thus exterminated.

PARKHURST, New York.

FIGHT AGAINST PROSTITUTION. F. SAMBERGER, *Ceska dermat.* **1**: 65 and 89, 1920.

The author discusses the question, Shall prostitution be regulated or abolished? from the standpoint of a venerologist, and one who expresses his opinion on the subject at a moment when a new state (Czechoslovakia) was formed and the country was to formulate new laws. Samberger states that the regulation system is not doing what is claimed for it. He opposes regulation, and advocates abolishment of regulated prostitution. The strictly med-

ical supervision cannot render prostitution safe. The best a regulation system can do is to leave at large all prostitutes who know how to use douches properly and to confine those with active syphilitic lesions. It is impossible to improve regulation beyond that.

CEPELKA, Chicago.

LARGE EPITHELIOMA OF THE NOSE, EYE AND CHEEK OF EIGHT YEARS' DURATION. L. QUEYRAT and RABUT, *Bull. Soc. franç. de dermat. et syph.* **2**:36, 1921.

The patient, a woman aged 69 years, presented an extensive ulceration involving the entire nose and the left eye with the adjacent cheek. The process had begun at the left inner canthus, and had spread gradually with no pain or constitutional disturbance. Radium treatment was advised.

Histologically it was thought to be a tubular-cell epithelioma arising probably from the sudoriparous glands. This is a great rarity. Darier reported a case in 1889.

PARKHURST, New York.

OUTLINE OF NEW LAW AGAINST SPREAD OF VENEREAL DISEASES. K. ULRICH, *Ceska dermat.* **2**:15, 1920.

The outline contains the measures taking direct action against venereal diseases and laws against prostitution. It is interesting to note that venereal diseases will not be reportable in the new republic, but the law will compel anybody infected to take treatments at his own or the state's expense; confinement in a hospital will become compulsory if instructions are not carried out; there will be a compulsory medical examination of suspects, and control after treatment.

CEPELKA, Chicago.

CASE OF ARGYRIA. BARTHELEMY and DANGLEMONT, *Bull. Soc. franç. de dermat. et syph.* **2**:46, 1921.

An old patient suffering with tabes of thirty-eight years' duration, had been given 144 gm. of silver nitrate in the form of pills during a period of fifteen years. The argyria had become manifest eighteen months after the treatment began. The head, neck and hands were most markedly involved, the rest of the body being of a brownish hue.

PARKHURST, New York.

TWO CASES OF LICHEN RUBER PLANUS CURED AT PODEBRADY (MINERAL SPRINGS IN BOHEMIA). T. VONDROVIC, *Ceska dermat.* **1**:132, 1920.

The effect of mineral baths containing free carbonic acid gas and iron salts on certain skin diseases (especially eczema, psoriasis, acne, furunculosis) is known to be beneficial. Lately two cases of lichen planus responded well to baths. It is undoubtedly the improved circulation in the superficial skin capillaries, stimulated directly by the free carbonic acid gas, and the maceration brought on by frequent, prolonged bathing that causes improvement. The radio emanation of the springs at Podebrady may also play a rôle. Baths control the itching promptly.

CEPELKA, Chicago.

A SYPHILITIC MANIFESTATION IN THE NOSE: REPORT OF TWO CASES. H. M. HAYS, J. A. M. A. **76**:1575 (June 4) 1921.

The failure of an engorged nasal mucous membrane, providing it is not polypoid, to shrink perceptibly under the application of a cocain-epinephrin solution is an indication for a Wassermann test. Two cases are reported in which lack of response to this test led to an investigation for syphilis with resultant positive findings. In each case proper therapy brought about complete relief.

MICHAEL, Houston, Texas.

SKIN AND VENEREAL DISEASES AMONG CZECHOSLOVAK ARMY IN SIBERIA. An. Tryb. **2**:11, 1920.

The army statistics show 3 per cent. of syphilitic and 12 per cent. of gonorrheal cases. The clinical source of syphilis did not differ from that in European cases. Hemiplegia during the first year was not a rare phenomenon, and occurred, without exception, in patients treated with insoluble salts or sublimate. There were scattered cases of iritis, facial paresis and malignant forms of lichenoid exanthems, mainly in the latter part of the first year. The majority of patients coming for intermittent treatment had syphilis latens. In treatment of syphilis the value of mercury rubs was again demonstrated. The variety of skin diseases was limited.♥

CEPELKA, Chicago.

AORTIC LESION IN A PATIENT WITH CONGENITAL SYPHILIS. M. PINARD, Bull. Soc. franç. de dermat. et syph. **2**:33, 1921.

In this case the involvement was demonstrated clinically, and the findings were verified by the fluoroscope. Syphilitic infection could be traced back to the grandparents if not farther, and it is also of interest that her parents were first cousins.

Leredde urges the importance of early recognizing and treating congenital syphilis.

PARKHURST, New York.

ECZEMA CAUSED BY ARTIFICIAL LEATHER IN HATS. KAREL HUBSCHMANN, Ceska dermat. **2**:140, 1921.

The author reports cases of dermatitis of the forehead caused by the bands in hats made of war leather substitutes which are usually impregnated with some irritant chemicals—phenol, tar and others. The dermatitis in mild cases appears as an itching erythema, in more severe cases as a papulovesicular eruption, often oozing severely. After the removal of the cause the dermatitis promptly responds to the usual treatment.

CEPELKA, Chicago.

A CASE OF ADULT URTICARIA PIGMENTOSA. WALLACE BEATTY, Brit. J. Dermat. **33**:138 (April) 1921.

This is a case report describing a case of urticaria pigmentosa in a man aged 32 years, the condition having been present for ten years.

SENEAR, Chicago.

CASE FOR DIAGNOSIS. S. E. DORE, Proc. Roy. Soc. **14**:80 (July) 1921.

A woman, aged 60, presented two small symmetrical patches on the extensor aspects of either forearm, of two months' duration on the left arm, and six weeks' duration on the right arm, consisting of a discolored center of a red or purplish color without induration, surrounded by hard raised pearly papules, which had apparently resulted from the breaking up of a continuous edge. The whole patch had the appearance of having evolved from a single raised lesion which had undergone involution in the center and spread at the periphery, and this course of events was confirmed by the patient. The diagnosis suggested was an unusual type of granuloma annulare; alternative suggestions put forward being those of persistent erythema and a manifestation of late syphilis.

Guy, Pittsburgh.

HEMORRHAGIC PURPURA FOLLOWING THE THERAPEUTIC ADMINISTRATION OF NEOSALVARSAN. THOMAS ANWYL-DAVIES. Brit. J. Dermat. & Syph. **33**:264 (July) 1921.

Twelve hours following the eighth injection of neo-arsphenamin in a combined course of antisyphilitic treatment with mercury and neo-arsphenamin in a case of latent syphilis in a woman 23 years of age, both soles began to swell; twenty-four hours later a rash appeared all over the body except the face, and was described by the patient as similar to "small dilated veins in the skin."

When seen a week later, dark purple petechiae covered the skin of the trunk and legs. The legs and thighs were covered with innumerable purpuric spots united by a network of dilated venules in the skin. Recovery took place within another week, and the general condition was good.

The author remarks that this condition may be similar to those cases of epileptiform convulsions following injections, in which postmortem examination shows punctuate hemorrhages in the brain.

SENEAR, Chicago.

THE CONSERVATIVE TREATMENT OF CERVICAL LYMPHATICS IN INTRA-ORAL CARCINOMA. D. QUICK, J. A. M. A. **77**:436 (Aug. 6) 1921.

The author does not believe in routine removal of the cervical lymphatics in cancer of the mouth. In early cases, there are two reasons for exercising judgment in the matter: 1. Many cases have no involvement of the lymphatic glands, and therefore their removal is unnecessary. 2. The cervical lymphatics perform a conservative function in the early course of the disease by acting as a barrier to dissemination, and their early removal takes away nature's chief obstacle to rapid spread of the disease.

Radium and roentgen ray should not be neglected in this disease and should be used in every case. A combination of surgery and radium offers more than surgery alone.

MICHAEL, Houston, Tex.

CASE OF SCHAMBERG'S DISEASE. S. E. DORE, Proc. Roy. Soc. **14**:80 (July) 1921.

A woman, aged 32, two months ago developed scaly brown patches on her knees which spread gradually to the upper parts of the thighs and downward to the ankles. It consisted of burned sienna colored patches and "cayenne

pepper" points, not disappearing on pressure, forming a continuous but patchy eruption extending over the anterior tibial regions and the anterior surface of the thighs, with scattered lesions on the posterior and lateral aspects. Among the patches, especially on the legs, were some superficial dilated venules, but no large varicose veins. There was some itching at first, but this ceased after the use of a mild astringent lotion. The appearance seemed to correspond in every particular to the peculiar progressive pigmentary disease described by Schamberg.

Guy, Pittsburgh.

LICHEN PLANUS IN CHILDHOOD. OSKAR KIESS, *Dermat. Ztschr.* **33**: 140, 1921.

The author reviews all the bonafide cases of lichen planus in children from birth to the age of 15 years. Eighty-nine cases are detailed and summarized according to nationality, sex, age, etc. The youngest patient was said to have had the disease when an infant 2 weeks old, and was seen when 11 weeks old. The etiology has never been clear. Nervous origin, infection, hereditary and familial influences have each been accredited. The eruption takes on about the same sites of localization as in adults. The type of linear lichen planus seems more prevalent among children. Ten questionable cases of lichen planus in children are given in detail.

This exposition is forty-four pages long, and there is a bibliography of 160 titles.

GOODMAN, New York.

LUPUS ERYTHEMATOSUS WITH SCLERODERMA. J. H. SEQUEIRA, *Proc. Roy. Soc.* **14**:75 (July) 1921.

A woman, aged 35, who had previously been under treatment for lupus erythematosus was presented with a scleroderma of the hands. The dorsal surfaces of the fingers and thumbs were purplish and the skin was immobile and could not be pinched up. The patient felt cold intensely and blisters developed continually on the tips of the fingers. Sensation was normal. The Wassermann reaction was negative, but calcareous glands were detected at the root of the lungs. Lately there had developed an erythematous scaly patch over the right mandible. The patient had received polyglandular extracts without benefit.

Guy, Pittsburgh.

A NOTE CONCERNING INTRAVENOUS INJECTIONS OF HEXAMETHYLENAMIN IN THE TREATMENT OF SYPHILIS. POMARET and THINH, *Ann. de dermat. et syph.* **7**:317 (July) 1921.

This method, which was recommended by Demitresco at Bucharest in 1920, was thought to be of possible value in cases in which arsenical and mercurial treatment were contraindicated. The authors administered it as advised, in a series of ten daily injections of 3 gm. each, to two patients with active secondary manifestations; there was not the slightest improvement. Both cases soon cleared up under treatment with arsphenamin.

Urotropin is therefore a useless weapon against syphilis.

PARKHURST, New York.

EXPERIENCE WITH PREGL'S IODIN SOLUTION IN DERMATOLOGICAL PRACTICE. KARL SCHREINER, *Dermat. Ztschr.* **33**:191, 1921.

This solution contains iodids and free iodin. It may be given intravenously in large doses. The effect on gonorrhea was not uniform when used alone, but when diluted with 2 per cent. boric acid solution, the results were better. In syphilis no remarkable results can be recorded. It is known that iodids have no spirocheticidal effects. In tertiary syphilis, the use of the solution intravenously and locally gave a more rapid clinical recovery than when used intravenously alone.

GOODMAN, New York.

THE GENITAL CHANCRE IN ITS RELATION TO SYPHILIS. M. DEL SEL, *Prensa med.* **7**:343 (May) 1921.

Sel insists that special care must be taken in diagnosing a genital chancre. He calls attention to the increasing number of syphilitic chancres and the decreasing number of chancroids or soft sores. It may be, he thinks, that after all there are no chancroids or they are exceedingly rare. He cites numerous instances in which clinically a chancroid was diagnosed as typical, verifying the diagnosis by a negative dark-field examination, but that later the patients developed secondary infections, or years after presented tertiary manifestations.

PARDO-CASTELLO, Havana.

MYCOSIS FUNGOIDES D'AMBLEE. J. K. MAYR, *Dermat. Ztschr.* **33**:185, 1921.

Mycosis fungoides d'emblée (Brocq-Vidal) is a form of the disease not so widely known as the classical form (Alibert-Köbner). The tumor stage of this form usually comes on without the premycotic or prefungoid, or the order may be reversed. There is an accompanying eosinophilia. The diagnosis depends on the clinical character and histologic findings. Tissue must be studied from the depth of the lesion to get the characteristic cellular change. The superficial tissue has a certain homogeneity lacking in the deeper tissue. Metastases often assume a sarcoma-like appearance in cell construction, and the skin lesions may have similar sarcoma aspects.

GOODMAN, New York.

CULTURE OF TRICOPHYTON GYPSEUM FROM THE BLOOD IN A CASE OF TINEA PROFONDA WITH LICHEN TRICOPHYTICUS. A. AMBROSSOLI, *Gior. ital. d. mal. ven.* **57**:233 (June) 1921.

Ambrossoli recovered the fungus from the blood of a patient with a kerion celsii of the scalp and an extensive eruption of the skin. The cultures were made in Sabouraud's maltose and glucose mediums. The author concludes that tinea profunda is a systemic disease and the lichen tricophyticus is due to the diffusion of the fungi and their toxins through the circulation.

PARDO-CASTELLO, Havana.

SYPHILIS A RURAL PROBLEM. W. J. HIGHMAN, *J. A. M. A.* **77**:583 (Aug. 20) 1921.

The recognition and treatment of syphilis have not yet been mastered in a degree commensurate with public needs. While the larger cities have their

quotas of accredited syphilographers, the smaller communities and rural districts are not adequately supplied with physicians who are prepared to treat the disease according to modern standards.

Expert mastery of the disease can only be acquired by long training, but competent knowledge can be attained after three months' study at a syphilis clinic. Such clinics are now found in practically all cities of 100,000 or more people.

Medical centers should arrange courses in syphilology especially adapted to the needs of the general practitioner, and the latter should prepare himself for the proper treatment of the syphilitic patient.

MICHAEL, Houston, Tex.

TUBERCULOSIS OF THE SKIN. J. H. STOWERS, *Proc. Roy. Soc.* **14**:85 (Aug.) 1921.

Photographs were presented of a man with an extensive tubercular involvement of the skin of the entire right cheek. The disease was of five years' duration and had been practically cured by means of picric-brass preparations combined with heliotherapy. Dr. Whitfield, in discussing the case, stated that the method of treatment had been tried and found wanting by many of the more experienced members, and he considered that it might be discarded.

GUY, Pittsburgh.

A CONDITION RESEMBLING LUPUS PERNIO IN A CHILD. F. PARKES WEBER, *Proc. Roy. Soc.* **14**:77 (July) 1921.

A boy 2½ years old presented an erythematous, swollen, in places scaly or telangiectatic, skin on the face, hands and feet. He also had an eczema from which an acid-fast organism was said to have been isolated. The tips of some of the fingers had been lost by gangrene or ulceration and trophic ulcers were present on the feet. Dr. Sequeira, in a discussion, associated the case with a condition called erythro-edema by Dr. Swift of Adelaide and reported recently in the *Medical Journal of Australia* by Dr. Jeffreys Wood. He considered the condition a toxic one.

GUY, Pittsburgh.

A CASE OF SECONDARY SYPHILIS TREATED BY INTRAVENOUS INJECTIONS OF HEXAMETHYLENAMIN. RAVAUT and RABEAU, *Ann. de dermat. et syph.* **7**:320 (July) 1921.

Eleven daily injections, exceeding the recommended dose, failed to influence the disease, and active spirochetes were readily found at the end of the series. Arsphenamin and mercury were then employed, giving immediate relief. Even as an accessory in the treatment of syphilis, hexamethylenamin seems to be worthless.

PARKHURST, New York.

SCLERODACTYLIA. J. H. SEQUEIRA, *Proc. Roy. Soc.* **14**:75 (July) 1921.

A woman, a machinist, aged 50, who gave a history of numerous whitlows in early life, had noticed swelling of the hands two months before presentation. The swelling persisted about a month and then disappeared spontane-

ously, leaving the fingers stiff. The skin over the hands, wrists and fingers was hard and fixed. Isolated sclerodermatous lesions were present on the forearms and chest.

Guy, Pittsburgh.

PYRETHRUM DERMATITIS: A RECORD OF THE OCCURRENCE OF OCCUPATIONAL DERMATOSES AMONG WORKERS IN THE PYRETHRUM INDUSTRY. C. P. McCORD, C. H. KILKER and D. K. MINSTER, J. A. M. A. **77**:448 (Aug. 6) 1921.

Pyrethrum is the most commonly used household insecticide at this time. The active insecticidal ingredient is not definitely known, but the flowers from which the powder is manufactured contain resins, oils, camphors, etc., which have irritating properties.

The authors have observed an occupational dermatitis among workers in this industry. It occurs on exposed parts as an erythematous, vesicular or papular eruption, accompanied by intense pruritus. Removal of the cause and soothing applications lead to speedy disappearance of the disease.

MICHAEL, Houston, Tex.

DIPHThEROID ULCERATION OF THE SKIN. E. G. GRAHAM LITTLE, Proc. Roy. Soc. **14**:83 (Aug.) 1921.

A woman, aged 40, had a chronic ulceration affecting the nose with a deep sulcus on the right nostril which was usually covered with scabs. Syphilis and tuberculosis were considered in the diagnosis and ruled out. A bacteriologic study revealed the presence of a diphtheroid organism. The presenter stated that specific vaccine therapy would be instituted thereby proving or disproving the diagnosis.

Guy, Pittsburgh.

A CASE OF DIPHTHERIA OF THE PENIS, WITH PARALYTIC SEQUELAE. COCHRANE, Brit. J. Child. Dis. **208-210**:86 (April-June) 1921.

Three days after an appendectomy, a boy of 3½ years developed an inflammation of the penis, which was incised; a gray membrane soon covered the glans, yielding Klebs-Loeffler bacilli. Cultures from the abdominal wound and from the nose and throat showed no bacilli. The source of infection could not be found. Recovery ensued.

PARKHURST, New York.

PECULIAR SCARRING FOLLOWING COMEDO. S. E. DORE, Proc. Roy. Soc. **14**:87 (Aug.) 1921.

A girl, aged 19, presented numerous small deep scars scattered sparsely over the nose and cheeks, some of them triangular or irregular in shape. There were also a few comedones. The scars seem to be the result of atrophy of the comedones without an intermediate stage of inflammation or suppuration, the above having been under observation for some years. The scarring was not of the close pitted cribriform variety described by French and American authors.

Guy, Pittsburgh.

A NEW CASE OF PACHYDERMIE VORTICELLEEE OF THE SCALP.
LENORMANT, *Ann. de dermat. et syph.* **7**:312 (July) 1921.

To supplement his recent report (*Annales* **5**:225 [May] 1920), the author describes a second case lately seen by him. In a child of 9½ years the occiput was occupied by a practically hairless, raised furrowed nevus patch, present since birth. The growth was excised at one operation, skin grafts being subsequently employed, with a good result.

PARKHURST, New York.

MULTIPLE IDOPATHIC PIGMENTED SARCOMA (KAPOSI). J. H. SEQUEIRA, *Proc. Roy. Soc.* **14**:86 (Aug.) 1921.

A man, aged 55, of English birth and parentage, presented typical lesions of this condition on the dorsal surfaces of his feet, together with isolated lesions on the left calf and left upper arm and the right half of the soft palate. The pathologic report was that of the richly pigmented (iron) angiomatous granuloma.

GUY, Pittsburgh.

DIPHThERIA OF THE SKIN. AGNES SAVILL, *Proc. Roy. Soc.* **14**:77 (July) 1921.

A girl had a crusted ulcerative lesion on the tip of the nose for four years. The diphtheria bacillus had been isolated, and antitoxin and vaccines had been used therapeutically with improvement. An alternate diagnosis of lupus vulgaris was offered. Dr. MacCormac said he had seen the case four years ago and had considered the condition lupus vulgaris, the presence of the diphtheria bacillus, which was noted at that time, being considered accidental.

GUY, Pittsburgh.

MODIFICATION OF THE GRAVITY METHOD OF ADMINISTERING ARSPHENAMIN. S. G. GILL, *J. A. M. A.* **77**:464 (Aug. 6) 1921.

To the usual gravity apparatus is added a rubber bulb with a valve at each end and a glass barrel at the tube outlet. The flow may be regulated by the bulb; and the glass barrel allows for the use of a small needle and indicates, by the appearance of blood in it, that the needle is in a vein.

MICHAEL, Houston, Tex

MYCOSIS FUNGOIDES. GEORGE PERNET, *Proc. Roy. Soc.* **14**:83 (Aug.) 1921.

A man, aged 55, was presented with a general erythroderma. The disease was almost universal, there being a few areas of normal skin about the trunk. The case was presented to show marked improvement, the result of quinin sulphate administered, 3 grains, three times a day.

GUY, Pittsburgh.

TRANSVERSE SEGMENTATION OF SPIROCHAETA PALLIDA. E. POLECK, *Dermat. Ztschr.* **33**:203, 1921.

In examining organisms from a known chancre, Poleck observed an organism of twenty coils divide transversely into two organisms of eight or ten coils each. He gives sketches of six phases of the division.

GOODMAN, New York.

A SIGN OCCURRING IN CASES OF TABES COMPLICATED BY CHARCOT JOINTS. L. ELOESSER, J. A. M. A. **77**:604 (Aug. 20) 1921.

Occasionally, a painful Charcot joint is encountered. This apparent paradox is explained by the fact that the skin is sensitive while the bone is analgesic. A pin thrust through the skin over such a joint will elicit pain; thrust to the bone, it may be moved around without calling forth any painful sensation.

MICHAEL, Houston, Tex.

ADENOMA SEBACEUM. E. G. GRAHAM LITTLE, Proc. Roy. Soc. **14**:84 (Aug.) 1921.

A girl, aged 15, who had had the eruption since early childhood presented the characteristic semitranslucent small tumors over the cheeks, in the nasal sulcus and on the nose. The majority of the lesions were of the red (Pringle) type, but there were also several of the pale (Balzer) type. In addition, there were several soft fibrous padlike colorless patches on the skin over the sacrum.

GUY, Pittsburgh.

A CASE OF CONGENITAL ICHTHYOSIS. C. H. DEAN, J. A. M. A. **77**:465 (Aug. 6) 1921.

This paper consists of a report of a case of persistence of the epitrichial layer. Two months after birth, the skin was apparently normal.

MICHAEL, Houston, Tex.

EXPERIENCE IN MASSACHUSETTS AND A FEW OTHER PLACES WITH SMALLPOX AND VACCINATION. J. E. HENRY, Boston M. & S. J. **185**:221 (Aug. 25) 1921.

This article gives a valuable statistical study of smallpox and vaccination in Massachusetts and Boston from 1702-1921, proving the effectiveness of vaccination.

LANE, Boston.

GRANULOMA ANNULARE. E. G. GRAHAM LITTLE, Proc. Roy. Soc. **14**:76 (July) 1921.

A boy, 12 years of age, had isolated sago-like lesions arranged in a ring. Dr. Little said that he regarded this as the first sign of the disease. He considered the condition as having tuberculous associations.

GUY, Pittsburgh.

A CASE OF SCLERODERMA GUTTATA. LOUIS SAVATARD, Brit. J. Dermat. & Syph. **33**:266 (July) 1921.

This clinical note reports an extensive case of scleroderma occurring in a man 46 years of age, only the hands, soles, face and scalp being unaffected. The early lesions were soft papules of pin-head to split pea size, while older lesions showed a central depression with a slightly raised edge. The oldest lesions were rounded, dead white, with minute blood vessels hedging them around, smooth on the surface and slightly depressed.

SENEAR, Chicago.

Society Transactions

SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MADRID

Regular Meeting, April 1, 1921

DR. AZÚA, *Presiding*

ACNE KELOID. Presented by DR. SAINZ DE AJA.

The patient had been treated with radium. There was a recurrence of a linear keloid lesion with the hair growing in the typical brush shape.

ARSPHENAMIN ERYTHEMA. Presented by DR. SAINZ DE AJA.

The patient had a general erythema, most prominent in the abdominal and dorsolumbar regions with some uncommon pigmentary lesions so far not described. At first it seemed an atypical form of lupus erythematosus, but this diagnosis was discarded because of the lack of fever and the spontaneous disappearance of the lesions. These exanthems may take different forms. In the benign types it is not necessary to stop treatment, but just to lengthen the intervals between injections, while in the general and permanent varieties treatment must be stopped.

DISCUSSION

DR. CRIADO mentioned another case of erythema in a patient with tertiary syphilis, who was treated first with mercury and then with arspenamin. At the seventh injection the skin reddened and developed an erythema which had lasted six months. Treatment was stopped. The patient returned in a year. One injection of 0.30 c.c. was administered, and the reddening appeared again. He intends to continue the treatment. A permanent erythema will undoubtedly develop in which condition the patient will be presented at the next session.

DR. BEJARANO stated that there are two sensitive types: one type is sensitive to small doses and another to excessive doses. He asked whether a blood examination had been made in the case of the patient previously reported because some patients, like the one reported by Aja, who had extensive gland enlargement, might be leukemic.

DR. AJA promised to make a blood analysis.

CASES FOR DIAGNOSIS. Presented by DR. PORTILLA.

New studies were made of the condition of the child presented for diagnosis at the last session. The fixation of complement with hydatid fluid proved negative, both with the blood and cerebrospinal fluid. Both parents gave a Wassermann +++ reaction. He showed a roentgenogram of the skull made by Dr. Calatayud showing increased thickness of the bones in the basilar and frontal regions. The patient received no treatment for three weeks and his condition grew much worse. He then received five injections of 0.15 c.c. of neo-arsphenamin which was followed by an improvement of the general con-

dition, nervous symptoms and speech. All these data suggest the syphilitic nature of the disease and a possible bone involvement. Dr. Portilla did not wish to express a definite opinion until the treatment had been completed, but he had no hesitation in stating that the patient's life did not seem to be in immediate danger, and the completeness of the cure depended on whether the process was secondary or tertiary. In the latter case there might be some sequestrums and some of the symptoms might become permanent.

SYPHILIS OF THE BRAIN. Presented by DR. BEJARANO.

Dr. Bejarano presented a man with syphilis of seven months' duration, which was neither diagnosed nor treated until secondary symptoms appeared. Then he received six injections of neo-arsphenamin and six of mercurial (gray) oil, whereupon the manifestations disappeared. After a month he began to suffer with intense occipital headache, which compelled him to remain in bed. One morning on awakening there was pronounced dizziness which kept him from moving; he also had complete left facial paralysis, diplopia, buzzing of the ears and decreased hearing on the left side. On examination there were found left facial hemiparesis, no loss of sensitiveness in either trigeminal zone, a slight convergent strabismus, hardly noticeable anisocoria, normal pupillary reflexes, ataxia of both upper and lower extremities, an ataxic gait with a tendency to propulsion and right orientation and no change in sensitiveness. The continuous intense occipital headache persisted, increasing in the evening, as well as the dizziness which prevented the patient from remaining alone.

Examination of the cerebrospinal fluid revealed definite hypertension, a + Wassermann reaction with 0.2 c.c. of spinal fluid and a +++ reaction with 0.5 c.c. of fluid; the Nonne-Apelt test was +; Pandy test, traces; the Noguchi test was negative, and there was 0.64 per cent. of albumin.

The treatment so far has consisted of two doses of neo-arsphenamin of 1.15 and 0.30 gm., respectively, and 12 c.c. of mercuric cyanid in six injections. This has caused the diplopia to disappear, and the headaches to become less pronounced. On the other hand, ataxia has progressed so that the patient must remain in bed. Dr. Bejarano drew two conclusions from this case: (1) the uncertain therapeutic outlook when patients have reached the secondary stage without receiving treatment, and (2) the rarity of early cerebral syphilis as a form of neurosyphilis since few other cases than those of gummatous lesions have been reported.

DISCUSSION

DR. BEJARANO: In reply to an inquiry by Dr. Barrio de Medina as to the final outcome, Dr. Bejarano stated that the ataxia had almost cleared up after fourteen injections of silver arsphenamin, making a total of about 2.20 gm.

DR. SAINZ DE AJA stated that the treatment received by the patient, consisting of seven injections of neo-arsphenamin and seven of mercurial (gray) oil, was insufficient as recently earlier recidives had been observed. Therefore larger doses are necessary. Either the drug has decreased in power or the disease has changed. He has also observed that patients with secondary syphilis with nervous foci are not cured entirely by the intravenous treatment and cerebrospinal injections are necessary.

DR. CRIADO gives courses of 5 gm. continuing the mercurial treatment without any interval. Three months later a Wassermann test is made and, regard-

less of result, the treatment is repeated. He does not believe in the magna sterilizatio mentioned at first. He does not stop treatment while the disease is active.

DR. PORTILLA recalled a case presented in previous sessions as an instance of the relative inefficiency of present arsenicals. In a year a patient had received two complete series of neo-arsphenamin and one of silver arsphenamin, twenty-five injections of soluble mercury and a course of mercurial oil. When the last series was completed a lesion developed (the patient had had no sexual relations) in which Arcaute found spirochetes and which was interpreted by this society as a Talman syphilid. He immediately started another course of neo-arsphenamin and mercurial oil, the patient having received so far eight injections of the former and nine of the latter. The lesion is not entirely healed yet, and the patient has active syphilitic lesions after having received in over a year of treatment three courses of neo-arsphenamin, one of silver arsphenamin, two of mercurial oil and a rather long course of soluble mercury. This, in Dr. Portilla's opinion, may be due either to the decreased activity of present products or to the decreased sensitivity to the drug of the spirochetes which have had several passages through arsphenaminized bodies.

DR. BEJARANO stated that the essential point was to establish a minimum total dose for each course. He thinks it should not be less than 5 gm.

MULTIFORM ERYTHEMA CAUSED BY GOLD AND POTASSIUM CYANID. Presented by DR. SAINZ DE AJA.

The patient was the same person with Kaposi's discoid erythematous lupus of Devergie's chalky type whom Dr. Barrio de Medina presented at the previous session. He received three weekly injections of 1 and 2 c.c. of gold and potassium cyanid and when the eighth was reached he developed a multi-forme dermatitis with erythemato-papular spots and pemphigoid lesions that involved the mucous membranes, causing edema and fever. The cyanid was stopped and the dermatitis cleared up gradually under a restricted diet and dusting powders. The urine was normal. The lupus disks grew worse at the height of the reaction, but when this yielded, the lupus lesions improved in an extraordinary manner, as little medication had been given. He recalled that a case of this cyanid complication had already been reported, but he wished to insist on the fact that some foreign writer had stated that gold compounds produce stomatitis equivalent to those produced by mercurials. Besides the oral manifestations, other skin symptoms develop, as in this patient. If one looks only at the mouth, one may call it stomatitis, although there is no foulness. The stomatitis is not due to poisoning, that is, excess of medication, since it develops after the first injection and other patients who have received a large quantity of drugs have not developed this condition. It is not identical with mercurial stomatitis.

VENEREAL CHANCER TRANSMITTED BY HEALTHY PERSONS.

DR. SAINZ DE AJA.

Dr. Sainz de Aja spoke of a couple who had been married five days when the wife developed venereal chancres. On examining and questioning the husband, he stated that he had never had a venereal disease. Dr. Aja reported this case in support of others previously recorded in which healthy persons transmitted venereal chancres. This also shows the important rôle played by healthy carriers.

Dr. Criado mentioned the survival of yenercal chancres outside the lesions; and Dr. Bejarano insisted on the need of microscopic tests in the carrier.

DR. BARRIO DE MEDINA, Secretary.

NORTHWEST GERMAN DERMATOLOGICAL SESSION

Held at Rostock, July 24, 1921

THE BASAL MEMBRANE AND STRUCTURE OF THE COVERING EPITHELIUM. DR. FRIEBOES.

Dr. Frieboes bases his report on two of his papers published in volumes 31 and 32 of the *Dermatologische Zeitschrift*. He discusses the question of the existence of the basal membrane and the structure of the covering epithelium. He says that there exists no membrane between the basal cell layer and the subepithelial collagenous tissue, for if there did the skin, in his opinion, in spite of its elasticity would be rigid, the exchange of nutritives would be rendered more difficult, and furthermore the membrane, if its contents of fluid were augmented, would be impossible to stain. Instead of the cell-membrane, he assumes that there is an entangled layer of fibrils which only appear to be a membrane when the fibrils surrounding the basal-cell domes are very short. If the zone of fibrils is disentangled a gradual disappearance of membrane is seen. The connection between the basal cell layer and the subepithelial collagenous tissue is formed according to his idea by entanglement of protoplasmic projections of the basal cells with part of the collagenous fibrils which stretch toward these. Furthermore, the prickle layer does not consist of separate cells but represents, in his opinion, a framework of protoplasm similar to the syncytium. Frieboes also believes that the skin is not a purely ectodermal formation but is developed from two germinal leaves, ectodermal and mesenchymal. To control these observations, Unna's method of staining epithelial fibrils should be used.

DISCUSSION

In the discussion which followed Frieboes' ideas were not acknowledged as correct. Unna holds that by using his original staining method the cell boundaries are not stained, but only the epithelial fibrils.

TREATMENT OF SYPHILIS IN GERMAN SOLDIERS AND NATIVE LABORERS IN SMYRNA DURING THE WAR. DR. FELKE.

Dr. Felke discussed his experiences in treatment of syphilis in German soldiers and native laborers in Smyrna during the war, compared with results of treatment of soldiers at Rostock (Germany). In Smyrna, 65 per cent. of secondary cases became negative after one course of treatment, in Rostock only 31 per cent. became negative. As the soldiers had been very poorly fed in Germany during the war, he concludes that the defensive action of the body is an important factor in the cure of syphilis.

KAPOSI'S SARCOMA OF THE SKIN. DR. BRANN.

Dr. Brann showed that histologically Kaposi's sarcoma of the skin is not purely sarcomatous but is a sarcomatous as well as angiomatous type.

DYSMENORRHEA SYMMETRICA OF MATZENAUER. DR. MEYER-
CLASSEN.

Dr. Meyer-Classen demonstrated two cases of dysmenorrhea symmetrica of Matzenauer. Both patients showed hypoplastic uterus, while the menses had never existed in one and had been very weak and at long intervals in the other. He also demonstrated a symmetric exanthem in an hysterical patient, which had an artificial origin, yet very much resembled Matzenauer's disease.

An interesting case of acrodermatitis Herxheimer was also demonstrated. This showed a scleroderma developing on the atrophy. A case of cured rhinoscleroma was shown; this patient had been treated with roentgen rays for several sessions of 30 X with a 5 mm. filter and 20 X with a 5 mm. filter.

AHLWEDE, Secretary, Hamburg.

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Archives of Dermatology and Syphilology

VOLUME 4

DECEMBER, 1921

NUMBER 6

THE TREATMENT OF EARLY SYPHILIS*

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In the treatment of early acquired syphilis we have to deal with two unequal groups. The larger is made up of the physically fit, the smaller consists of individuals with damaged organs, arteries or tissues, due to age or to disease.

Such may be the condition when syphilis is acquired. It is necessary, therefore, as soon as the diagnosis has been made to ascertain by thorough physical examination in which group the patient belongs. This division is more essential today than formerly, for we now aim at a radical cure in early cases. This means the use of more potent remedies than of old. The synthetic drugs which are supposedly parasitotropic may be organotropic as well, and the toxic effect of mercury on the tubules of the kidney is well known. These conditions play an important part in the management and care of all, but especially of the physically unfit.

The syphilologist today has a dual responsibility—first, in curing his patient and, second, in safeguarding the public against contagion. The application of modern methods to the first part of the problem does much toward controlling the second part.

With the discovery of *Spirochaeta pallida* as the cause of syphilis, the application of the dark field as a ready means of demonstrating the organism and the introduction of the synthetic arsenicals in the treatment, the management and care of primary syphilis have been reduced to the lowest terms. The care of primary syphilis today is essentially the treatment of the disease as a whole. Certain unusual initial lesions may require special attention on account of some prominent feature, such as pain, size, contamination or location. Constitutional treatment is usually all that is needed to heal the primary sore, but as a protection to others a local mercurial should be applied.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

The important feature of primary syphilis is its prompt recognition, which means the protection of associates and the institution of treatment at the time most favorable to the individual for a radical cure. An early diagnosis is not usually difficult if one possesses a reasonable clinical knowledge, considers the possibility of syphilis and follows the suspicion with a careful microscopic examination. Failing to demonstrate spirochetes in smears from the primary sore, puncture and aspiration of the satellite bubo may obtain serum showing the organisms. Neisser¹ obtained spirochetes at the time of the appearance of the primary sore from the satellite bubo, bone marrow and the spleen. This shows the uselessness of excision of the initial lesion with a hope of aborting or changing the course of the disease.

At various times, both here and abroad, arsphenamin has been given as a prophylactic to persons with a known exposure (confrontation). The records of these results are scanty. Metchnikoff established the efficiency of mild mercurous chlorid ointment as a prophylactic, but to be effective it must be applied within a few hours after inoculation. The work of Brown and Pearce² has shown that the dissemination of spirochetes from the point of introduction is very rapid; they have been able to demonstrate organisms in the regional lymph nodes in less than forty-eight hours after inoculation. They also found spirochetes in the blood stream before a primary lesion was recognizable at the site of inoculation. The excision of the scrotum, testicle and wide zone of tissue outside the point of inoculation, forty-eight hours after this procedure, failed to prevent the development of syphilitic lesions in ten rabbits used in the experiment. Michel and Goodman³ have used arsphenamin as a prophylaxis and report their cases, about thirty in number, some of which date back two years. Active syphilis in the partner was proved. Treatment consisted of from three to six injections at two to five day intervals, the average dose being 0.3 gm. of arsphenamin. No patient treated in this way has developed a positive Wassermann reaction or signs or symptoms of syphilis, and they have all been kept under observation long past the incubation period. Furthermore, they quote Fournier and Guenot's⁴ report on the abortion of syphilis with arsphenamin

1. Neisser, quoted by Hazen, Henry H.: Textbook on Syphilis, St. Louis, C. V. Mosby Co., p. 53, 1919.

2. Brown, Wade H., and Pearce, L.: Note on Dissemination of *Spirochaeta Pallida* from Primary Focus of Infection, Arch. Dermat. & Syph. **27**:470 (Oct.) 1920.

3. Michel, L. L., and Goodman, H.: Prophylaxis of Syphilis with Arsphenamin, J. A. M. A. **75**:1768 (Dec. 25) 1920.

4. Fournier and Guenot: Presse méd. **27**:554 (Oct.) 1919.

used during the incubation period on forty women who had been exposed by intercourse with syphilitics having genital lesions (diagnosis confirmed by a positive dark field examination). In all but five patients (in whom the primary lesion was less than ten days old) the Wassermann reaction was strongly positive. The women were all symptomatically and serologically free from syphilis. Prophylactic arsphenamin was given from a few days to three weeks after exposure. No preventive measures had been used. Five women similarly exposed refused treatment and later developed syphilis.

Not one of the forty treated with arsphenamin or neo-arsphenamin has shown a sign or symptom of syphilis and all have remained Wassermann negative. Twenty of the women have been under observation over three years. They received from 1 to 1.2 gm. of arsphenamin or from 1.2 to 2 gm. neo-arsphenamin.

Is this the opening of a new field in preventive medicine?

A positive diagnosis is still a required antecedent of treatment but, thanks to modern methods, this should be possible several weeks before the onset of the second stage. Confrontation and serologic examination may contribute to our early positive knowledge. The syphilographer knows the strong and weak points in the methods of precision, but many patients with primary syphilis first consult their family doctors; and the early use of mild mercurous chlorid on a sore that is said to be "nothing" negatives a subsequent dark field, or a too early negative Wassermann reaction is accepted without question.

A product of our modern methods of diagnosis and treatment is the pseudo-syphilographer. To him the clinical study of syphilis is unnecessary. The public Wassermann laboratory makes the diagnosis without cost and a few injections of arsphenamin clear up the lesions, and the patient, believing himself cured, considers the incident closed, until he suffers a relapse or shows evidence of cerebrospinal syphilis. We know now that the foundation of late manifestations in the brain cord and arteries is laid during the early months if not weeks of the disease, therefore their prevention is accomplished by thorough treatment of primary and early secondary syphilis. There is every reason to believe that the inadequate use of the newer arsenical preparations will be followed by an increased number of cases showing cerebrospinal involvement over the number of patients treated with less effective remedies, administered over a period of years. With this in view, there is great need of an expression of what may safely constitute a minimum amount of treatment for our early cases. Whatever the approved course may be for a so-called routine it must be flexible, carefully supervised, and frequently changed to meet the indi-

vidual conditions. In the early infectious stages with open lesions, one would rightly take greater risks than later when there are no infectious lesions present and not the same promise of a radical cure. Cases of patients with active pulmonary tuberculosis acquiring syphilis illustrate the first group. Another class calling for great care in treatment is the cardiovascular (arteriosclerosis). Persons showing damaged kidneys should have a renal function test before receiving mercury and arsphenamin. Of the original list of contraindications given by Ehrlich (optic atrophy, pregnancy, advanced heart and kidney disease), perhaps a low renal function today commands our greatest respect.

It has been shown that both arsphenamin and mercury are liable to produce a mild or severe kidney irritation, particularly of the tubules; therefore frequent examinations of the urine must be made while these drugs are being used. Investigation has shown that of the two, mercury is more likely to cause severe renal irritation or inflammation. A careful study may be necessary to determine whether one is dealing with a syphilitic albuminuria or nephritis, or just a renal irritation due to antisymphilitic remedies.

The liver is another viscus that is apparently more frequently damaged by the modern than by the old methods of treatment. Jaundice has long been recognized as of syphilitic origin during the secondary stage and is usually catarrhal in character. Cases of syphilitic acute yellow atrophy are on record in which all other causes were excluded.⁵ There has been a decided increase in the number of patients with jaundice during the past two years. The condition appears most often after the arsphenamin injections are finished and during the course of intramuscular injections of mercury. Many of the cases have shown only a mild catarrhal jaundice, and recovery has been complete on stopping the mercury and giving the usual care. There are severer cases; rarely one has gone on to the condition of typical acute yellow atrophy. I think it possible to prove by arithmetic that these cases are due to the arsenic and mercury; both minerals have long been recognized as possible causes of the condition. We have seen two such cases, but the pathologist was unwilling to state definitely the cause, saying that it was the same condition as that seen after the administration of phosphorous, toxemia of pregnancy, etc.

According to Brooks,⁶ severe myocarditis may be a very early manifestation of syphilis. He has reported about twenty-five cases,

5. Senator and Engel-Reimers: Quoted by Taylor, R. W.: *Venereal Disease*, 1895, p. 760.

6. Brooks, H.: Paper read before Suffolk Dist. Med. Soc., Boston, 1921.

two of which were fatal before the appearance of secondary manifestations, the diagnosis of syphilis being made at necropsy.

A statement was brought to my attention which asserted that during the war many of the cases of men dropping in the ranks, either after severe drilling or forced marching, were due to early acute syphilitic myocarditis. With a view to determining the frequency of this myocardial change, we have had special examinations, made by an internist from the cardiac clinic, of about forty cases of early syphilis. His findings so far have been at variance with those of Brooks. In no case examined has myocarditis been found. The search is still going on.

Having made the diagnosis of early syphilis, one must choose his course. Where there are no infectious lesions, treatment may well be started with a few intramuscular injections of mercury before beginning the arsphenamin. When infectious lesions are present, the need of protecting others outweighs any disadvantage to the patient from the immediate administration of both drugs.

The advocates of arsphenamin therapy alone have few followers; therefore most patients receive combined treatment of arsphenamin and mercury. "Intensive" is the term frequently applied to the treatment of syphilis today and it apparently has a different meaning for different men. Biweekly or every-other-day injections are considered by some as intensive; but the term should be applied only to the method advocated by Pollitzer,⁷ which consists of a full dose of arsphenamin given intravenously on three successive days. These are followed by six weekly injections of an insoluble mercurial. At the end of the sixth injection of mercury, three more daily injections of full doses of arsphenamin are given and these, in turn, are followed by six more injections of mercury. There are figures to show⁸ that following this line of treatment a higher percentage (28 per cent. more) of negative blood Wassermann reactions were obtained at the end of the ninth week than by the alternate day and less frequent injections. However, at the end of twenty weeks the advantage is with the less frequent injections. These observations were based on the study of 106 cases, of which 80 per cent. were negative by the tenth week, 98 per cent. by the sixteenth and 100 per cent. by the twentieth. Clinical results were the same with the different methods, but the margin of safety is greatest with the less intensive course.

This undoubtedly accounts for the more widespread popularity of the less intensive regimen under which the patients get from twelve to fifteen weekly injections of mercury, and the tendency has been to increase the number of arsphenamin injections in the initial

7. Pollitzer, S.: *J. Cutan. Dis.* **34**:633 (Sept.) 1916.

8. Chargin, L.: *Antisyphilitic Therapy: Comparative Study of Some Intensive Methods*, *J. A. M. A.* **76**:1154 (April 23) 1921.

course from six to eight or more. The size of the dose averages 0.4 gm. of arsphenamin or its equivalent for a man weighing 150 pounds. Whatever the plan of action for the first course of mercury and arsphenamin, treatment must not be discontinued on the first appearance of a negative blood reaction. Medication may be omitted for a month or two, and then a second course of arsphenamin and mercury should be given as before, only with a shorter course—from four to six injections of arsphenamin and eight or ten of mercury. If the Wassermann reaction is still negative, and the patient clinically well, a vacation of three or four months may be allowed, when more mercury, with or without arsphenamin should be given, and a Wassermann test made six months later. Before discharging the patient, an examination of the spinal fluid should be made.

There is everything to gain and nothing to lose by giving short courses of mercury through the first few years after the Wassermann is negative and the patient without signs or symptoms.

The consensus of opinion of syphilographers favors arsphenamin over neo-arsphenamin in the serologic effect, while they seem to agree that the clinical results show little if any difference. The greater ease of preparation, the toleration in concentration, the greater freedom from reactions immediate and remote, and the possibility of using neo-arsphenamin many times in the same vein, even though a small one, makes neo-arsphenamin a valuable and permanent addition to our antisyphilitic remedies. However, neo-arsphenamin is not without its dangers. The first fatal case that came under my observation was in a consultation a day or two before the end, which came twelve days after the last of three weekly injections of the original German neo-arsphenamin. The patient, who weighed less than 115 pounds, received 0.9 gm. at each injection. A sparse macular eruption developed over the dorsal surfaces of the hands and feet after the second injection. This warning was unheeded, and 0.9 gm. was given a week later. This was followed within two hours by an intense general erythema with jaundice. From that time on, a severe dermatitis of a pemphigoid type developed. The urine was negative until a short time before the end.

Nitritoid reactions are much less frequent with neo-arsphenamin but when they do occur are often more severe than those occurring with arsphenamin.

According to Schamberg,⁹ there is not the danger of precipitation in the blood and pulmonary embolism with neo-arsphenamin that there is

9. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Weiss, Charles: Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-arsphenamin, *Arch. Dermat. & Syph.* 1:235 (March) 1920.

with arsphenamin. This occurrence has been put forward as a cause of certain reactions at the time of the injection. The intense colicky pain in the location of the kidneys which Schamberg believes due to a vasoparesis and which often comes after the flushing has passed in the nitritoid reactions is more frequent with arsphenamin.

It is generally recognized that oxidation greatly increases the toxicity of both neo-arsphenamin and arsphenamin, owing to the formation of "arsenoxid." Hunt¹⁰ has carried out a series of careful experiments on rats to determine if possible the toxic substances. He found that warming and standing often decreased rather than increased the toxicity of certain lots of arsphenamin. Cold may preserve the toxicity for long periods. He states that the symptoms (in rats) produced by the presence of "arsenoxid" are very characteristic—struggling, convulsive movements, lashing of tail, rigidity of legs, irregular respiration, protrusion of the eyes and lachrymation. Roth¹¹ has shown that by shaking neo-arsphenamin or alkalinized solutions of arsphenamin in the presence of air even for one minute increased the toxicity 60 per cent. Hunt¹⁰ found great variation in the effect of aeration of different preparations, some becoming markedly toxic within an hour, while others became so only after four hours. Hunt feels that it has been assumed in experiments, rather than actually demonstrated, that increased toxicity was due to oxidation. He states, "My experiments offer a certain amount of proof that the oxid, or at least partially oxidized but at the same time easily reducible substance, is the chief factor." If Hunt is right, why may not some of the obscure reactions that follow quite promptly the intravenous injection be due to the rapid oxidation that must take place as the drug is being injected, going as it does directly to the best oxidizing plant in the system, the lungs?

It has been shown with animals that the method and rate of injection plays an important rôle in the reactions; therefore the rate of injection in man should be slow, about five minutes for an injection of arsphenamin and a shorter time (two minutes) for neo-arsphenamin. A friend of mine said that in a large civic hospital in France he saw neo-arsphenamin given in great concentration (0.2-3 c.c.) and injected in the fraction of a minute with no apparent reactions or complications.

In the widespread use of arsphenamin today, most patients are given injections and allowed to go their way with instructions to eat

10. Hunt, R.: Some Factors Relating to Toxic Action of Arsphenamin. *J. A. M. A.* **76**:854 (March 26) 1921.

11. Roth, G. B.: *Pub. Health Rep.* **35**:2205 (Sept. 17) 1920.

lightly after the lapse of several hours and to remain quiet (directions that are probably most often ignored). There is no doubt that if the individual who is to receive an intravenous injection is prepared as for a surgical operation and given a saline the next morning, eating lightly, many reactions will be avoided. The reactions occasionally occurring during or immediately following the injection are: vomiting, rapid pulse, changes in color (pallor and flushing) dilated pupils, perspiration and a feeling of apprehension or prostration. They are probably due to some gastric or other condition of the patient entirely aside from the arsphenamin as the vomitus consists of large amounts of slightly digested food at such a remote period from ingestion as to show clearly some marked disturbance of digestion. May not these reactions be due to a splitting up of the arsphenamin by the products of delayed digestion? A sense of heaviness and tingling in the fingers and hand of the injected arm often precedes a nitritoid reaction or may simply mean a slightly overalkalinized solution.

During the past year, I have used both in private and hospital practice a fairly large amount of sodium arsphenamin made by the Diarsenol Company of Buffalo. It is said to be arsphenamin with the proper amount of sodic hydrate added during the process of manufacture to form the disodium salt of arsphenamin, which has been found by investigation to be less toxic than the monosodium salt.

It possesses the advantages of neo-arsphenamin in the ease of preparation and there have been practically no immediate reactions. The only real disadvantage so far noted has been a tendency to develop nausea, which may not appear until twenty-four hours after the injection and may last for from twenty-four to seventy-two hours. The likelihood of this nausea developing can be almost eliminated with free saline catharsis the morning after the injection. There has been no tendency to phlebitis following repeated use of the same vein nor has there been experienced the pain in the shoulder during the injection that is sometimes felt with arsphenamin, especially if the solution is overalkalinized.

It being essentially the same solution as arsphenamin, there is the same need of avoiding extravasation.

For some time silver arsphenamin has been used in Germany and, within the past year, in this country. It is undoubtedly too soon to give it a proper relative value. Its claims for recognition are greater spirocheticidal and therapeutic action. As a few cases of argyria have been reported, it seems too early to pass on this possibility, which, if only of rare occurrence, would constitute a serious handicap.

The consensus of opinion seems to be that silver arsphenamin, as the other arsenicals, should be used in conjunction with mercury.

Monarsone, galyl and soamin are some of the other organic arsenicals that have been advocated at times in the treatment of syphilis. Nichols¹² has shown that monarsone has no spirocheticidal effect, and therefore no place among antisymphilitic remedies.

The therapeutic test, the old time friend of the clinician, has been reinforced by the synthetic arsenicals. One still sees an occasional case with suspicious clinical signs, with negative serologic and roentgen-ray findings, in which the response or failure following two or three injections of arsphenamin is sufficient evidence to establish the diagnosis beyond a reasonable doubt.

One seldom sees a syphilitic manifestation of skin, mucous membrane or periosteum (and perhaps some of the visceral lesions may also be included) that does not respond to three injections of arsphenamin.

While this procedure is usually of greater service in late cases, there are probably few here who have not seen patients on whom needless surgical operations had been performed on tongue, lips or tonsils, for unrecognized primary syphilis.

From a public health standpoint, too much emphasis cannot be laid on the importance of early recognition of extragenital primary lesions, as their location usually prevents suspicion of the real nature of the trouble and therefore no precautions are taken. The syphilographer of today must be versed in all the various manifestations and the results of tests, and he must be able to direct the patient, if not to recognize or diagnose all the finer manifestations in the different organs (eye, ear, viscera, etc.). He must also go beyond the individual, and seek out and bring under treatment as many donors or recipients of infection as possible.

In this as in the general follow-up, the assistance of trained medical social workers is most essential. These workers require especial training as they are frequently called on to handle most delicate and difficult situations with parents, employers, the courts, probation officers, societies for the care of girls, prenatal clinics, lying-in hospitals and homes for unmarried pregnant girls. This requires tact, patience and understanding, for there is always danger of arousing antagonism. Compulsion can never take the place of compassion!

The treatment of many cases of early syphilis is complicated by economic problems that often require considerable skill and perseverance on the part of the social worker. Most of these patients are perfectly capable of working, if loss of time from their job does not cost them their positions.

12. Nichols, H. J.: The Spirocheticidal Value of Disodium Ethyl Arsenate (Mon-Arsone), *J. A. M. A.* **76**:1335 (May 14) 1921.

We conducted a study at one time which showed that hospital fees, car fares and medicines just about equaled the wages lost on account of the time spent in attending the hospital, and at that time (1914) amounted in round numbers to \$100 a year. Hazen's¹³ figures are practically the same. The amount today is probably greater as the items are all higher than in 1914.

The vast majority of early syphilitic patients are and must be treated as ambulatory patients, but there should always be a certain number of beds available for the very infectious and the incorrigibles. The study of the spinal fluid must be made, and interesting or unusual conditions must receive attention.

There are now few conditions that absolutely preclude the possibility of using arsphenamin, providing the details of preparation and supervision of the patient are faithfully carried out. We learned, during the war period of shortage, that results followed much smaller injections than were formerly given, and the tendency since has been to increase the number rather than the size of the doses. One scarcely sees any clinical evidence of "arsenic-fast" strains of spirochetes, though this possibility must constantly be borne in mind.

The various theoretic fears of disaster from the simultaneous administration of arsphenamin and mercury have not been substantiated, and we usually finish our early treatment by giving mercury. There can be no doubt that Hutchinson with gray powder and Fournier with protoiodid obtained actual cures in a certain percentage of early cases.

Neurorecidives are scarcely seen since a policy of shorter intervals between the arsphenamin injections has been carried out.

Very small, infrequent injections seem to stimulate a renewed activity on the part of the spirochetes along the line of the observation of Bronfenbrenner and Noguchi¹⁴ that small amounts of arsphenamin in the mediums stimulated the growth of spirochetes in vitro. Bronfenbrenner and Schlesinger¹⁵ demonstrated a similar effect on animals with experimental syphilis.

These observations must be kept in mind with the tendency toward smaller doses. I believe this is especially important in early syphilis. From the clinical standpoint we have long felt the importance of beginning treatment as early as possible, and the results of study of the

13. Hazen, H. H.: Text Book on Syphilis, St. Louis, C. V. Mosby Co., 1919, p. 27.

14. Bronfenbrenner and Noguchi: J. Pharmacol. & Exper Therap. **50**:333, 1913.

15. Bronfenbrenner and Schlesinger: Proc. Soc. Exper. Biol. & Med. **18**:94 (Dec.) 1920.

spinal fluid are entirely in accord. Moore¹⁶ reported his findings on the spinal fluid of 642 patients in all stages of syphilis, but without demonstrable physical evidence of neurosyphilis. The fluid was studied after from two to six months of treatment. In thirty-four patients in whom treatment was begun in the primary stage, only one (2.9 per cent.) showed an abnormal fluid (amount of treatment not stated).

After the establishment of the second stage, the incidence of abnormal fluid was about the same (12-15 per cent.) regardless of the length of time the disease had existed or by what sign it was apparent. Of his 642 patients; only 12.7 per cent. showed an abnormal fluid. This would seem to show that the treatment given had cleared up more than half the cases, as the observations of other investigators show a much higher percentage of positive fluids in untreated cases, some as high as 65 per cent. or positive fluids in early secondary syphilis, without symptoms of cerebrospinal syphilis.

There can be little doubt that, at the height of the infection, which may be taken as the early part of the second stage, the central nervous system in a very high percentage of the cases, as well as the other organs and tissues of the body, is invaded by spirochetes. That tabes or paresis develop in only a comparatively few cases goes without saying.

Moore's figures confirm the value of thorough early treatment. He states that every patient should have a spinal puncture at the end of the first or second course of arsphenamin, and it should be repeated at least once before the patient is discharged as presumably cured. This is undoubtedly a most admirable procedure, but very difficult if not well nigh impossible for us, with only a small number of beds at our disposal. So far there is no uniform opinion that it is an entirely safe procedure to perform lumbar puncture on patients and send them home at once. In spite of all precautions and the use of a small gage needle, occasionally the terrific postpuncture headache occurs, which acts as a strong deterrent toward routine spinal puncture in ambulatory patients.

There are certain manifestations of syphilis in the early stages which may call for special treatment.

Alopecia of the scalp, brows and lashes, is not often seen when treatment is begun in the primary stage. The constitutional treatment is usually sufficient. In some cases a stimulating wash with mercuric chlorid may be of service.

16. Moore, J. E.: Cerebrospinal Fluid in Treated Syphilis, *J. A. M. A.* 76:769 (March 19) 1921.

Wile's¹⁷ observation of the high percentage of changes in the cerebrospinal fluid of patients showing alopecia is interesting. In forty-six cases with this symptom, 73 per cent. showed an abnormal fluid. He suggests that alopecia may be due to a disorder of enervation associated with coincident cerebrospinal involvement rather than a direct spirochetal involvement of the hair follicle.

In iritis full dilatation of the pupil and energetic constitutional treatment is usually all that is necessary. The use of iodids in addition to mercury and arsphenamin is often of value in relieving pain, promoting absorption and shortening the attack. As changes in the fundus (choroiditis, etc.) may occur, it is advisable to have the assistance of an ophthalmologist. Here again Wile's observations are of interest. Iritis was noted in twenty-one of 508 patients with secondary syphilis. Of these twenty-one cases, fifteen or 71.4 per cent. showed cerebrospinal involvement. One of our latest cases of severe iritis was treated by combined intravenous and intraspinal injections and made an unusually rapid recovery.

Nocturnal headaches and periosteal pains seldom call for special treatment. If arsphenamin cannot be used at once potassium iodid will generally afford relief.

Mucous patches and ulcerated papules of the skin are now seldom seen, thanks to prompt treatment, and thereby one of the greatest menaces to associates has been removed.

Pregnant patients with early syphilis should receive as energetic treatment with arsphenamin and mercury as their condition will permit. Careful watch of the kidney function must be maintained. I have never seen harm result from the use of arsphenamin in pregnancy, and the beneficial effect on the fetus is striking. Infants closely approaching the normal are frequently seen when dead born or badly diseased babies seemed inevitable. Furthermore the danger to nurses and associates is greatly diminished. Many cases of accidental infection about the face in adults has been traced to the fondling of congenitally syphilitic babies. These asymptomatic infants, even with a negative blood Wassermann reaction, should be kept under observation for a long time, as potentially syphilitic.

In a recent textbook on syphilis, the author of the chapter on syphilis of the eye states, "Where most was expected of it, arsphenamin has singularly failed, namely, in interstitial keratitis. . . . In nearly all cases where it has been used, the second eye has become involved; hence it does not seem to have even a prophylactic effect."

17. Wile, U. J., and Marshall, C. H.: *Arch. Derm. & Syph.* **3**:272 (March) 1921.

This statement is so entirely at variance with our experience that I most earnestly ask you to try arsphenamin in interstitial keratitis and judge the results. We began using it with a few children in 1912 and, since 1916, have given either arsphenamin or neo-arsphenamin in practically all of the cases that we treat in conjunction with the Massachusetts Charitable Eye and Ear Infirmary and in private.

During the two years from June, 1919, to June, 1921, we treated 134 cases with the following results: 99 had 20/30 vision or better, 12 had 20/70, 5 had 10/100 vision or less, and 18 had been under treatment too short a time to include them in our group.

It is true the second eye may develop the inflammation during treatment, but if so it responds to the continued injections as promptly as the first and the end-result is just as good. There have been but few relapses after the treatment was completed, which is quite an improvement over the old lines, and the vision tests are much higher. At first the ophthalmologists were skeptical, but the results have won their support. In no case has the eye condition been aggravated by arsphenamin. Pain, photophobia and lachrymation are usually benefited after a few injections. Mercury with chalk and syrup of hydriodic acid are given in addition to the arsenic. Local treatment with atropin and yellow mercuric oxid is carried out at the Massachusetts Charitable Eye and Ear Infirmary. These cases have received from five to fifteen intravenous injections at weekly intervals. In some cases, better results have appeared to follow the use of neo-arsphenamin, but there is no marked difference in effects. Some of these children were totally blind when treatment was begun, and no scarring of the cornea now remains. The ages have varied from 4 to just under 50.

As would be expected the earlier in the attack the arsphenamin is given, the prompter the response. Several (twenty-eight) of the children have shown the symmetrical synovitis of the knees, in many ways a condition strikingly analogous to that of the eyes. Several children with swollen knees had been treated for a long time with plaster casts for supposed tuberculosis, and the development of the corneal inflammation first suggested the possibility of congenital syphilis, although the roentgenograms were always negative, showing no bone pathology, a condition strongly suggestive of these syphilitic joints.

The minimum of treatment for a case of primary or early secondary syphilis should consist of: (1) mercurial dressings to initial lesions; (2) intravenous arsphenamin, 0.1 gm. to 40 pounds body weight, repeated in from 3 to 5 days, and then at five day or weekly intervals until six to ten injections have been given; (3) full doses of mercury, preferably by intramuscular injection; if an insoluble salt, fifteen injections should constitute the first course, and (4) frequent examinations of the urine. Following the mercurial injections, an

interval of five or six weeks should elapse before checking up with the Wassermann test. If it is positive, the first courses should be repeated. If negative, a vacation of three months is allowed, at the end of which time ten or twelve mercurial injections and from four to six of arsphenamin are given. With a second negative Wassermann reaction, during the following six months from six to eight mercurial injections are given, and during the next year the patient should receive short courses of mercury.

An examination of the cerebrospinal fluid should be made early in the disease if possible and certainly before the patient is discharged.

Patients with organic disease who acquire syphilis are to be treated with the same or greater consideration than patients showing the same sort of damaged organs of syphilitic origin.

A PRELIMINARY REPORT ON THE THERAPEUTIC ACTION OF SILVER ARSPHENAMIN *

JOHN A. FORDYCE, M.D.

NEW YORK

Silver arsphenamin, which has been in use in Europe for more than two years, is now made in this country and was distributed for clinical purposes in October, 1920. Since that time 168 patients, to whom about 1,800 doses were given, have been treated in my service at the Vanderbilt Clinic and the City Hospital.

Silver arsphenamin is the sodium salt of silver-diamino-dihydroxy-arseno-benzene and is produced by the action of silver salts on arsphenamin. It is a brownish black powder, soluble in cool water, alkaline in reaction, and containing about 20 per cent. of arsenic and 14 per cent. of silver. At first it was given in a dilution of 1:50 and later reduced to 1:40 per 0.1 gm. It may be given in greater concentration, but more dilute solutions were preferred because the drug in this way is introduced slowly by the gravity method, a very important factor, it was found, with the older remedies, in preventing table reactions. The dosage employed in the beginning was 0.1 gm. for men, gradually increased to 0.15 and then 0.2 gm. Now the initial dose is 0.1 to 0.15 gm. for women and for men 0.2 gm., the latter sometimes receiving as much as 0.3 gm. It should be borne in mind, of course, that the treatment must be individualized, and that the condition of each patient really determines the dose. The intervals, too, have been reduced from a week, in early active syphilis, to four or five days, for the first few doses, or even closer intervals, according to the activity of the case and the amount of the drug used. Eight to ten injections have constituted a course. In the majority of clinic cases, mercury was not administered in addition, but when there is no contraindication, such as in nephritis, mercury should be utilized in combination, especially in early cases. Owing to a conservative attitude in the beginning, patients did not receive an adequate amount of silver arsphenamin, and it is difficult, therefore, to make an accurate comparison with the other arsenicals, especially as many of the cases were difficult to control, in spite of follow-up work, after the active symptoms had disappeared.

* From the Department of Dermatology and Syphilology, Columbia University, College of Physicians and Surgeons.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

The 168 patients treated may be grouped thus:

CASE GROUPS

Primary Syphilis.—Four patients with chancres, which had been present from five days to a week, had a positive dark-field and a negative Wassermann reaction. The four lesions healed after two injections, and the blood reaction continued negative under treatment. These patients receive the same amount of treatment as those with early secondary syphilis.

Beginning Secondary Syphilis.—Ten patients presented a chancre, a positive dark-field and a weakly positive reaction. The chancres disappeared after from one to three injections. No further clinical manifestations made their appearance and the Wassermann reaction, in all ten cases, which was tested after eight injections, was negative.

Secondary Syphilis with a Four-Plus Wassermann Reaction.—Thirteen patients had no skin or mucous membrane lesions. Three gave negative reactions when examined after the ninth injection; eight who are still under treatment, and who have had from four to seven injections, have not yet been reported on; two patients disappeared after the second and fifth injections, respectively.

Secondary Syphilis with Eruption and a Four-Plus Wassermann Reaction.—Thirty-five cases. Skin rashes and mucous patches we found usually disappeared after the second or third injection. Six patients have received two courses of ten injections each, and the reactions have been negative since the first series. Eleven patients have received from six to sixteen injections, and the reactions are negative. The reactions of eight patients at the completion of the first course of from eight to ten injections were still ++ or ++++. Four patients have not yet completed their first course. Six patients failed to return after receiving from two to seven injections.

One of the patients, at the completion of his first course of treatment, neglected to return as instructed. He came to the clinic first Feb. 3, 1921, with a maculopapular rash and a four-plus blood Wassermann reaction, and attended regularly, receiving ten injections of 0.2 to 0.25 gm. biweekly. May 20, 1921, he presented himself with two penile lesions, the one a small ulceration with an indurated collarette, the other herpetic. They were in entirely different locations from his first sore. The dark field showed an abundance of spirochetes in both lesions. He admitted exposure two weeks previously. Blood taken on that day for examination was negative with all methods.

Another case worthy of mention is that of a young married woman, pregnant seven months, who came to the clinic with a secondary papular rash and four-plus blood Wassermann reaction. She was given six

injections of from 0.15 to 0.2 gm., at intervals of from five days to a week. She entered the Sloane Hospital, and was delivered of a healthy, seronegative child. Three weeks later she reported at the clinic, at which time her blood, as well as the infant's, was negative.

At the clinic, our experience has been that fully two thirds of persons having early florid syphilis gave negative reactions at the completion of their first course of ten injections of arsphenamin reinforced by mercury.

Latent Syphilis.—In all twenty-seven cases were treated. They were asymptomatic but had strongly positive Wassermann reactions. The disease had been present for periods varying from three to fifteen years. Five patients showed a reduction from four-plus to degrees varying from three-plus to plus-minus after from four to fifteen injections. Four patients who had given a three-plus or a four-plus reaction were negative after from six to ten treatments; one of these again became three-plus three weeks later. The condition of nine patients remained unchanged after from eight to thirteen injections. Two of these patients had received numerous injections of arsphenamin and mercury previously.

Nine patients failed to return after receiving from two to ten injections.

Tertiary Syphilis.—Nine patients with gummas were treated. These lesions healed after from three to five injections.

One case which had been two-plus was negative after the eighth injection; six were still four-plus at the completion of their first course; two discontinued treatment after the third and ninth injections, respectively.

Two patients with tubercular syphilids gave prompt clinical response; the seroreaction in one was still four-plus after eight injections; in the other it was three-plus after the sixth.

Fifty-six patients with neurosyphilis had been treated. These had old cases with tabes, paresis or cerebrospinal syphilis. The majority of them had received arsphenamin or neo-arsphenamin before. No difference in the therapeutic action between this drug and the older ones was noted clinically, and it is too early to form any judgment as to its effect on the serology. The serum of patients treated with silver arsphenamin was used for the Swift-Ellis intraspinal method and no greater reactions than those with the other preparations were noted. The main difference in the intravenous injections has been the greater tolerance of the patients to the silver product. Two table reactions were observed, the one in a tabetic who always reacted on the table to the other arsenicals. He had no difficulty after his first injection

of 0.1 gm., but when the dose was increased to 0.15 gm. he reacted as formerly. The other patient was a woman who at the completion of her sixth injection of 0.2 gm. gave the usual anaphylactic reaction.

Several cardiac cases with aortitis have also been treated. In two with well-developed aneurysms, no change was brought about in the condition. In the third improvement followed, and the patient was again able to resume his occupation.

COMPARATIVE TOXICITY OF THE ARSPHENAMINS

From animal experimentation in the laboratory, Corbett rates the efficacy of silver arspenamin as over twice as great as that of arspenamin and from three to five times that of neo-arsphenamin. Its toxicity as compared with the latter preparations he has worked out thus: A clinical dose of 0.6 gm. of arspenamin is equivalent to 10 mg. per kilogram in the dog. To produce a nephrosis in these animals, eight times the dose must be used, or 80 mg. With neo-arsphenamin, the clinical dose of 0.9 gm. would be equivalent to 15 mg. per kilogram; 75 milligrams is the smallest amount which will produce a nephrosis in dogs, that is, five times the usual dose. For silver arspenamin, 5 mg. per kilogram would be the equivalent of a clinical dose of 0.3 gm. Here it was found that from 75 to 100 mg. were required to bring about nephrosis or from fifteen to twenty times the dosage employed.

It would be fair to assume that the activity of arspenamin would be increased by reinforcement with the Ag component and this was shown to be the case in Kolle's experimental work with spirochetes. Whether clinical experience will confirm the laboratory results cannot be stated definitely as yet, as too little time has elapsed to make a statement as to duration of the cure.

IMMEDIATE REACTIONS

Immediate reactions after silver arspenamin have been rarer than after the other arsenicals. Among the 168 patients treated, table reactions were noted three times. They were of the usual nitritoid type, consisting of flushing of the face, injection of the conjunctivae, dyspnea, increased heart action and apprehension. They quickly passed over and were followed by no discomfort later. One of the patients had reacted severely each time also to arspenamin and neo-arsphenamin. Occasionally pain is complained of in the arm toward the termination of the injection. This is due to the irritating effect of the drug on the walls of the vein and it usually subsides promptly under the influence of heat. In one patient with very small, thin-walled veins, sclerosis followed.

LATER REACTIONS

Gastro-intestinal symptoms are much less frequent than after arspenamin and neo-arsphenamin. Silver arspenamin, therefore, makes a good substitute in cases in which the latter are not well borne. In five private patients, two men and three women, who had been particularly difficult to treat because of their intolerance to the older arsenicals, they reacting each time with a chill and prolonged vomiting, the administration of silver arspenamin was followed by no reaction in either man and none in one of the women, under a dosage of 0.15 gm. at weekly intervals. In the second woman, 0.1 gm. produced vomiting just once, and the third woman, who was pregnant, tolerated 0.1 gm., but vomited once or twice when this dose was exceeded.

Cutaneous complications so far have been noted three times. A woman with taboparesis, who was intolerant to arspenamin and neo-arsphenamin, owing to the development of severe dermatitis after very small doses of either, was given a little less than 0.1 gm. silver arspenamin. Two hours later she had edema of the face with closure of the eyelids and marked generalized pruritus, which persisted two days. The two other patients had a mild erythema of the face three days after injection, which quickly disappeared. Jaundice has occurred twice during treatment. In one, a man suffering from latent syphilis, the symptoms developed five weeks after his ninth injection (dosage 0.2 to 0.25 gm). The other case was that of a colored woman, also with latent syphilis, the jaundice appearing three weeks after her eighth injection (dosage 0.2 gm).

ADVANTAGES OF SILVER ARSPHENAMIN IN OBVIATING REACTIONS

The advantage, therefore, of this preparation as shown by clinical experience is, so far, its greater freedom from reactions. This, in the first place, is due to the diminished toxicity of the drug itself, and, secondly, to the ease of preparation, which probably insures a solution whose physical state is more nearly in accord with the requirements necessary to maintain the blood equilibrium when injected.

Table reactions, during or after an intravenous injection of any of the arsenicals, can in a large measure be obviated by the proper preparation and administration of the solution. While many of the reactions are of the nature of a true hypersensitization, which in some cases can be overcome by small desensitizing doses before the full amount is given, or a slow desensitization by the slow, continuous introduction of dilute solutions by the gravity method, others are due to bad technic. Recent work by Myers¹ would tend to show that the

1. Myers, C. N.: Development of the Chemo-Therapy of Organic Arsenicals and Related Physical Clinical Phenomena, *J. Lab. & Clin. Med.* June, 1921.

majority of immediate reactions can be explained on a physico-chemical basis. In a personal communication he states that in reactions occurring in the human body shortly after an injection, he believes the immediate effects are probably molecular, except in acute renal manifestations, and that nervous phenomena, acute fall in blood pressure, headache, coma, dyspnea, cyanosis and early death, and that host of symptoms classified under anaphylactic shock, are due to physical conditions of the solutions injected and of the blood stream. When injections in the form of the monosodium salt are made, the calcium and magnesium are removed in the nature of salts of arsphenamin. These salts are colloidal in nature and when "aggregated" are very insoluble.

When a solution is injected rapidly and under-alkalinized, in the case of arsphenamin, precipitates are formed which clog the capillaries and produce the acute manifestations. This is overcome by the use of the disodium salt, which tends to keep calcium and magnesium in solution, or by the slow injection which allows the body fluids to regain their equilibrium, or by the use of a dilute solution. The manner and the method of dissolving the drug determines in a large measure the physical solution of the drug, its viscosity and colloidal structure. The colloidal particles are entirely different in physical nature when a dilute solution is examined under the ultramicroscope as compared with a more concentrated one. If the solution is injected under these conditions, there is an aggregation of molecules whose diameter is too great to allow free passage through the capillaries. Colloids may be injected intravenously, but their diameter must be less than 2 microns. Myers has further shown experimentally that it was more satisfactory to allow the solution to stand for about thirty minutes in order to obtain the proper physical adjustment of the solution. In an experiment on rats in which he used the same solution but varied the time of standing, he found only one survival among twenty rats injected with from 100 to 140 mg. per kilogram immediately after mixing, and two deaths among fifteen rats after the solution had stood for one-half hour. Further, it was shown by animal experimentation that rapid injection with a syringe will cause immediate death.

ARGYRIA

The chief objection to the use of silver arsphenamin is the fear of producing an argyria. To date, more than a million doses of the drug have been given on the continent and about 125,000 doses in this country, and no authentic cases of argyria have been reported. The case mentioned by Lochte² was found, on investigation, not to have been

2. Lochte: *Therap. Halbmonatsh.* **34**:334 (June 15) 1920.

seen by him at all but was mentioned by him on the strength of a report made by a "naturopath."

Regarding the authenticity of this report, Dr. Scholl of Farbwerke, Hoechst on Main, states in a letter dated Dec. 2, 1920:

In the above mentioned publication Lochte makes a brief statement in which he cites references placed at his disposal by the "naturopath" regarding a case of supposed argyria after silver salvarsan injections and, using this case as a basis on his own behalf, cautions against the use of such products. Lochte expressly denies the authorship of the sensational heading "Argyria After Twelve Silver Salvarsan Injections," and states that the case report as sent to him bore this heading. Further, he states that he himself has not seen the case, although he requested that the patient call on him. He accordingly was not in a position to confirm the diagnosis of the naturopath, and he himself suggests the possibility of an arsenical melanosis.

Danysz, who in 1914 reviewed the work of Orfila, Charcot, Cruveilhier and others who were testing the physiologic and therapeutic action of silver salts on man, made the statement that no cases of poisoning, so-called, had been observed and that argyria was noted only after the absorption of 30 gm. of silver nitrate.

Sollmann,³ in his text, says:

The inorganic silver salts, especially the nitrate, are used to produce astringent, caustic and antiseptic effects. They form resistant precipitates with proteins so that their local action is easily controlled. The toxicity for higher animals is very low, and the antiseptic efficiency is high. Silver is not absorbed from the alimentary canal in sufficient quantity to produce systemic actions. Because of its precipitation by proteins and chlorid, even large doses of silver nitrate rarely produce serious poisoning. Long continued use results in argyrisms, and traces, probably organic, must therefore be absorbed. Argyrism develops gradually after prolonged internal or external use of silver, when the total dose has reached from 15 to 30 gm. The black granules do not consist of metallic silver for they are easily soluble in KCN and difficultly in concentrated nitric acid.

It is claimed that in the preparation silver arspnenamin the silver is present in the nonionic state, which would lead to the production of more soluble compounds than when the silver is present in the ionizable condition.

Myers found that animals receiving twelve times the clinical dose in a series of from twelve to fifteen injections excreted most of the silver within seven days, none of them retaining more than 25 per cent. On the basis of the limits worked out by Sollman, it would require 453 injections of 0.3 gm. of silver arspnenamin to bring out the cumulative effect.

3. Sollmann: Textbook on Pharmacology, 1918, p. 780.

CONCLUSIONS

Silver arsphenamin is a valuable addition to our remedies for syphilis because of its greater freedom from reactions.

Our experience to date is too limited to warrant an opinion as to its superiority in effecting a cure. This can only be determined when we have standardized its employment and observed it over a longer period. At present I feel justified in saying that it is as efficacious as the older remedies in causing cutaneous lesions to disappear, and my impression has been that in certain early cases it was perhaps more rapid in its action. The patients in whom negative reactions have been obtained have not as yet had a spinal fluid examination. Positive statements, therefore, cannot be made as to what the percentage of cures, with the dosage and intervals used by us, will ultimately be. While some of the continental physicians are giving as high as 0.5 or 0.6 gm. at a dose, until we know more about the drug I should not favor making the maximum dose at the present time greater than 0.3 gm..

ABSTRACT OF DISCUSSION

ON PAPERS OF DRs. SMITH, STOKES AND FORDYCE

DR. UDO J. WILE, Ann Arbor: It is my fortune or perhaps misfortune to see much more of visceral syphilis than of any other form. I wish to subscribe to the dicta so well expressed by Drs. Smith and Stokes that, both for early and late cases, not only is intensive treatment necessary, but such treatment must follow an intelligent review of each patient with regard to his general well being.

I cannot subscribe to Dr. Smith's statement that the cases of acute yellow atrophy occasionally seen in syphilis could be ascribed to the mercury and arsenic which had been used, because I have seen such cases develop before either drug had been used. In fact, these cases differ from acute yellow atrophy from either cause in that they are influenced favorably by antisyphilitic treatment.

I have seen at least one case in which maniacal symptoms had already set in, in which, following enlargement, rapid shrinkage of the liver had begun and in which recovery had taken place following specific treatment.

With regard to myocarditis, my experience coincides with that of Dr. Harlow Brooks. Such involvement may not manifest itself by the newer methods of investigation, such as the electrocardiograph, but careful examination will show irregularities of pulse rate, arrhythmia and occasionally heart block.

The only other possible issue with Dr. Smith lies in the question of the time at which a lumbar puncture should be done. In my opinion, it should not be done before the patient is discharged from custody, but before treatment is begun.

In connection with Dr. Stokes' remarks, his observations on the treatment of late visceropathies constitute facts not well recognized. In certain classes of cases we are confronted with the paradoxical fact that the patient recovers from syphilis but nevertheless dies. The explanation for this lies in the fact that such organs as the heart and liver, when subjected to antisyphilitic treatment, shrink so rapidly and are replaced by so great an amount of scar tissue that they are unable to function and their increasing shrinkage with time results in increasing disability.

DR. SIGMUND POLLITZER, New York: I regret that none of the readers of the papers have had any experience with my method. They would have been able to report, I am sure, that the method is as free from danger as any other. In the paper which Dr. Smith cited, published within the last few weeks, nothing is said about any unfavorable results, but its author draws out of the air the gratuitous statement that, as the method is theoretically more dangerous, it should be condemned. I may say after an experience of six years with it that so far as safety of the method is concerned, it is just as safe as any other. I do not wish to give the impression that all my cases are treated in one way. I am entirely in accord with what Dr. Stokes has said of the necessity of individualization in our treatment of syphilis. I am still of the opinion that my intensive method of treatment gives better results than the ordinary once-a-week method. I have never been able to see why a drug like arsphenamin, which produces a single sharp effect, should be given once a week except on the assumption that a divine Providence had divided time into weeks for our therapeutic convenience. Personally, I can find nothing sacred or reasonable in the seven-day period. We give insoluble salts of mercury once a week because we have found that in that way we can maintain a fairly level mercury content in the system. We give the soluble salts daily because, with their rapid elimination, daily injections are necessary if we would maintain the proper level. Arsphenamin is comparable to the soluble rather than to the insoluble mercurials, and I fail to see the scientific basis for administering a preparation of that sort at intervals of a week, which are too long from one point of view and too short from another. They are too long to keep up a uniform arsphenaminization of the blood over the period of the treatment and they are too short for a repetition of the spirocheticidal effect that we expect from arsphenamin. We should give the organisms that escape the first injection a chance to recover from the arsphenamin effect and to resume the motile form in which they are destroyed by arsphenamin. A week is apparently too short a time for these changes to take place; Ehrlich originally recommended a repetition of the injection after three weeks.

Dr. Smith misquoted me in saying that I repeat the first course of arsphenamin immediately after the treatment with injections of mercury. I invariably give the patient a period of rest of from four to eight weeks before repeating the courses of injections of arsphenamin and mercury.

DR. HARRY G. IRVINE, Minneapolis: I do not believe any case of early syphilis should be allowed to rest for three months. If you are sure of your case and it is cured by the first course, that will be all right, but I think in the ordinary case it is too long a rest period.

I agree with Dr. Smith about the importance of the follow-up work and social service. I feel that they are among the most important factors in the management of these cases, if not the fundamental factors. It should be emphasized that in that social work the physician has a definite field. He should not expect the social worker to do all of it. The beginning of it rests with the physician himself.

DR. ERNEST L. McEWEN, Chicago: In view of the work that has been done by some members of the Association on insoluble injections, I should like to ask Dr. Smith if he feels that there is any objection to the use of the insoluble salts of mercury by injection; and I should like to know what Dr. Stokes thinks about that method.

DR. WALTER J. HIGHMAN, New York: I was captivated by Dr. Pollitzer's views on intensive treatment and plead guilty to having made an attempt to carry out the treatment exactly as he has outlined it. In the few cases in which I have tried it, I can corroborate what he says about the lack of danger. I cannot agree with all he says about the importance of the method, even to the extent of carrying out the injections at biweekly intervals. I recall three or four cases which I saw in their early stages a year or so ago and have observed since. Two cases were those of a husband and wife. The husband was a powerful individual and the wife rather a frail woman. The husband had to leave for a trip soon after I saw him—his case was about six weeks farther advanced than his wife's. He received intensive treatment and his symptoms promptly disappeared. He returned from his trip in blooming health, but with a positive Wassermann reaction which has persisted since. His wife received the conventional treatment we have all been using for several years. Her Wassermann reaction was negative after eight injections of arsphenamin and twelve of mercury. She then became ill with a hip inflammation that orthopedists considered nonspecific. Her Wassermann test, which has been taken at regular intervals, has remained negative for a year and a half.

I had another patient who was treated every third day with arsphenamin until the man had received six or eight injections. He had a maculopapular eruption, a healed chancre and a + + + + Wassermann reaction. His Wassermann reaction became negative on the ninth day, a week before he started on a business trip. In March, 1920, when he returned, his Wassermann test, which I took as a matter of routine, was positive and I could not believe the report. I had another test made a week later but just prior to taking the blood for the second test I found that in the preceding five days a recurrent roseola had developed. Since then his Wassermann reaction has persisted.

It has occurred to me that with the more or less intensive treatment of syphilis, with anything that approximates Dr. Pollitzer's intervals, we do the patient a certain amount of harm in a field that we, perhaps, do not yet understand. In our early treatment of syphilis we have as a therapeutic adjuvant, if we do not overtreat, a native immunity which we might disturb or destroy by coddling the patient; by too intensive treatment we destroy the immunity. This may be a matter of theory, but it is worth weighing and the consensus of opinion as to the conventional treatment we have all followed for so long is that it is good, if not, perhaps, the best.

DR. HAROLD N. COLE, Cleveland: Dr. Stokes spoke about the late treatment curing the disease but killing the patient. I think the same thing applies to the early cases. I realize that we are to discuss the arsphenamin or arsenical treatment tomorrow, but right now I wish to say that I think there is more danger in Dr. Pollitzer's method than in the one ordinarily used. If a man has an idiosyncrasy, he will be put in more danger if he is treated every other day than if he receives the injections a week apart. That point should be considered. I have a patient who has received only three injections of the old arsphenamin, and those have been given a week apart. Immediately after the third injection, he developed a marked dermatitis, and if he had received injections a day apart I fear to think of what might have happened.

DR. WILLIAM ALLEN PUSEY, Chicago: I have nothing to say except to express my gratification at the general tone of the papers, and my very great

pleasure that we are still becoming more conservative, and allowing a larger importance to the human factor in the disease.

DR. SIGMUND POLLITZER, New York: In answering the question about dermatitis, I wish to say that, since 1915, I have not had a single case of exfoliative dermatitis following arsphenamin. Exfoliative dermatitis occurs only after a number of weekly injections—usually four or five—have been given and I believe that it is caused by the repeated insult in the skin. Where a single massive dose is given—because three full doses in three days is equivalent to that—and then a month or two is allowed to elapse, the possible injury to the skin has had an opportunity to wear off and the subsequent treatment does not have the deleterious cumulative effect that provokes the dermatitis.

DR. C. MORTON SMITH, Boston: In regard to what Dr. Wile said about acute yellow atrophy, we have seen more cases of jaundice during the last two years, since using more intensive treatment. Cases were reported in 1890 and quoted in Taylor's textbook in which all possible causes of acute yellow atrophy except syphilis had been ruled out. In our two cases that came to necropsy, the pathologist refused to say that atrophy was of arsenical origin.

As to myocarditis, we have felt for a long time that syphilitic myocarditis existed. However, since we have been making a special study of this condition no cases have occurred. I have no doubt that in time cases will be found.

In regard to lumbar puncture, if that procedure was as easy as testing the blood we would do it much oftener; but at the present time I think it is the consensus of opinion that performing lumbar puncture in the case of patients in an outpatient clinic and sending them home is unwise. We feel that we have done fairly well by performing lumbar puncture before the end of the treatment and earlier, as indicated. If we had the same number of beds at our disposal as Dr. Wile, we would do more spinal punctures.

Concerning the remarks of Dr. Pollitzer regarding Scholtz, his name does not appear in the manuscript. It was an interpolation. If I misstated, it was with no intention of condemning Scholtz or of robbing Dr. Pollitzer of the glory.

I have shared Dr. Cole's fear of dermatitis, feeling that arsenic was responsible. If this is true, the patients showing an idiosyncrasy to arsenic would have received three daily injections; as the dermatitis does not show for several days, the reaction would be much more severe than if the patient had received only one injection during that period.

Another argument for weekly injections is that the majority of patients are working, and it is much easier for them to obtain permission to be away once a week. This continues through their course of mercurial injections.

In regard to Dr. Irvine's objection to waiting three months, the Wassermann reaction is taken at the end of six weeks, after the mercurial injections, and if it is positive the courses are repeated. If it is negative, the rest period follows.

Regarding the soluble and insoluble salts of mercury, we have used for a long time a mercurial cream known as "Adams' cream" and have had no difficulty. Whether the preparation with hydrous wool fat and vegetable oil makes a difference I do not know, but we have had no difficulties from the use of the insoluble salt.

I am thankful for what Dr. Pusey said, because occasionally one sees cases which fail to respond to intensive treatment.

DR. JOHN H. STOKES, Rochester, Minn.: I feel that insoluble mercurial salts interfere with, rather than assist, intelligent intensive treatment, through their cumulative action. Their popularity has depended on their convenience rather than on their therapeutic efficiency. I have drawn up several charts illustrative of the cumulative injury to the kidney produced by insoluble salts, and the demonstrations of Dr. Cole with regard to mercurial (gray) oil should also be recalled. If a patient lives in an inaccessible place, or is negligent of treatment, insoluble salts are my last resort. I never use them without the conscious determination to establish an absorption depot. I have had no experience with water soluble salts in oil suspension.

I prefer inunction in the large majority of patients, and I believe that the majority of them can be induced to use it by a sufficient pressure from their medical advisor. The use of insoluble salts as part of any system combining two methods leaves one entirely in the air with reference to dosage and complications on account of the unknown quantity created by the absorption depot. Renal irritation and even hemorrhagic nephritis has occurred in several patients under our observation who had been managed by the so-called "red manual" technic. The soluble mercurial salts are prompt in action and noncumulative, and I use them by preference in neurosyphilis.

Gennerich has turned about rather suddenly regarding his early attitude toward arsphenamin, and has expressed himself as believing that it is a direct predisposing element to neurosyphilis. Recently in the abstract department of the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* there appeared an excellent review of Gennerich's remarks on that subject. I have tried to get the original brochure but have not yet succeeded in doing so. I think his view should receive much consideration. Those who have watched his work will agree that he has been in a better position to judge the effects of arsphenamin than any one else in central Europe. He has had his patients exceptionally well under control, and when he says that patients who have received mercury only are much less exposed to neurosyphilitic accidents than are those who have received arsphenamin, his views should have our respectful consideration.

We should make special mention of the gradual disappearance of criteria for cure. The Wassermann reaction has subsided into a position where no wise syphilographer guides his treatment entirely by it. The positive Wassermann reaction has been damned; the negative reaction has been damned. The demonstration of the occurrence of progressive visceral syphilis in patients with no other signs of the disease, the insignificance of manifestations in women, and the fact that reinfection may be only superinfection, as shown by Brown and Pearce's recent contribution on the production of a second chancre while the first was still in evidence, has cast doubt on the validity of cure. "Cure" is passing and in its place I think we should use the word "arrest." We should impress on each patient that his problem is not of a week, or of a month, or a year or five years, but that he is a candidate for observation throughout his life.

We should acknowledge also the wise conservatism of the stand taken by Dr. Pusey when arsphenamin was first introduced, in which he expressed the view, since borne out by much clinical and experimental evidence, that arsphenamin, by its interference with the mechanism of natural resistance in syphilis, might prove to be a danger under certain circumstances rather than a benefit.

DR. JOHN A. FORDYCE, New York: We have had too much theorizing and not enough of actual experience. If we see the patient when he has the early

lesions we should give two or three injections in the first week, and then gradually lengthen the interval, because there is a cumulative effect.

In regard to inunctions, I was trained many years ago in Hot Springs and we found the use of inunctions a very good method of treatment, but in private practice it is difficult to get a patient to use them. They are dirty and irritating and, if we give arsphenamin simultaneously, it seems to me that the mercury lowers the resistance of the skin. I have seen cases of generalized exfoliative dermatitis in patients who were using inunctions and receiving arsphenamin at the same time and I felt that in these patients the mercury had lowered the cutaneous resistance. We can obtain all the effects by using the mercury in oil. A grain of mercuric chlorid can be given every three or four days. We have done that repeatedly and have given from fifteen to twenty and sometimes thirty doses and have seldom seen any irritative effect on the kidneys. It is true that we see cases with a few casts or a little albumin, but they are the exception. Theoretically mercury damages the kidneys; actually it rarely does.

I agree with Dr. Smith as to treatment of keratitis. I have had a number of experiences in New York such as he has had in Boston. I remember the case of a patient with congenital syphilis who developed an acute keratitis, for which she was sent to the country. Her physician told her that fresh air and good food were of more value than treatment. I told her that in spite of fresh air and forced feeding she would have repeated attacks of interstitial keratitis. She then placed herself under treatment and has been free from any recurrence for three years. There is no question that arsphenamin is a valuable remedy in interstitial keratitis.

I would like to ask Dr. Stokes regarding his treatment of Charcot joints. I believe he made the statement that if we see these cases early enough we can prevent them. The difficulty is that we do not see them early enough; they come on over night. If we do recognize these cases early, what effect will treatment have? In the first place, we do not know what a Charcot joint is—whether it is a syphilitic infection of the joint itself or whether it is due to disease of the nervous system. I cannot quite accept Dr. Stokes' statement that it is possible to control a Charcot joint by early recognition.

Another point is the development of hypertension in syphilis. This was demonstrated in a physician who left us about six years ago, with a negative Wassermann reaction. He returned with an aortitis and a blood pressure of 215. This illustrates that these patients should be kept under observation. I think the question of hypertension deserves a good deal of consideration.

A RARE FORM OF SUPPURATING AND CICATRIZING DISEASE OF THE SCALP

(PERIFOLLICULITIS CAPITIS ABSCEDENS ET SUFFODIENS)*

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A chronic inflammatory disease of the scalp, primarily perifollicular, leading to suppuration and extensive undermining of the involved area, was given the name *Perifolliculitis capitis abscedens et suffodiens* by E. Hoffmann. He presented such a case before the Berlin Dermatological society, Nov. 12, 1907. Hoffmann's patient, a man aged 25, had then been afflicted for a year, and showed "on the occiput many (about 20) nearly hazelnut sized, pale, hemispherical elevations, hairless or covered at the borders with sparse, short hair stumps, from which on pressure pus exuded and into whose fistulous openings the sound could be introduced up to 4 or 5 cm. Beside these closely crowded tumors with smooth, pale, grayish-red surfaces, which gave the scalp a rough, uneven, mammillated appearance, there were a few disseminated pustules and crusts, pierced by hairs, and isolated, small coin-sized, smooth scars. Healing resulted in further scar formation and was hastened by a 10 per cent. sulphur-zinc paste. Microscopically there was no fungus; cultural investigation for sporotrichosis proved negative. There was, then, a suppurating folliculitis, undermining the scalp, with formation of fistulae and termination in cicatrizing alopecia."

The American, and to the best of our knowledge, the British, French and Italian literature contains no record of this entity; but in the German dermatologic publications we find that A. Ruete¹ has carefully described the disease in an article which deserves to be reviewed in detail. In the introduction he mentions the numerous processes leading to scarring of the scalp or to alopecia associated with scarring, touching on syphilis, tuberculosis, favus, lupus erythematosus and the innominate cicatricial alopecias of Besnier, which include folliculitis decalvans

* Read before the Section on Dermatology and Syphilology at the Seventy-Second Annual Session of the American Medical Association, Boston, June, 1921.

1. Ruete, A.: Ein Fall von *Perifolliculitis capitis abscedens et suffodiens*. *Dermat. Ztschr.* 20:901, 1913.

and the pseudopelade of Brocq. To this list he adds ulerythema sycosiforme, also the scarring and alopecia which succeeds furunculosis, and lastly what has been called "a deep form of acne decalvans," but is better designated, according to Hoffmann, as "perifolliculitis capitis abscedens et suffodiens."

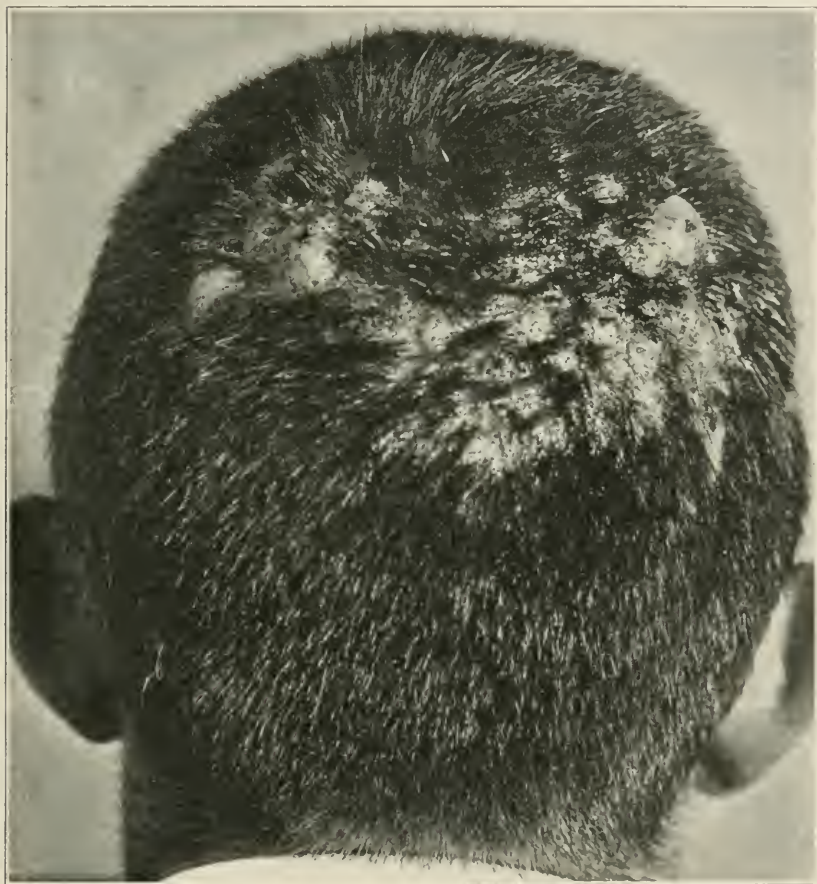


Fig. 1.—Numerous isolated and confluent serous and seropurulent, hemispheric lesions, with crust formation due to a serosanguineous exudate.

NOBL'S CASE

So little is definitely known about this last-mentioned process that Ruete published a detailed presentation and analysis of a case he had observed and treated. Before describing this case a brief review of similar instances is given. These are three in number, including Hoffmann's, already mentioned. Nobl, Oct. 26, 1904, presented a case before the Vienna Dermatological Society, which showed a deep folli-

culitis of the scalp with baldness: "In a man of 34, the vertex and adjacent occiput were the sites of nodules, isolated and grouped, hemp-seed to pea sized, reddened and partly faded, projecting above or level with the skin, whose summits were occupied by loose, easily detachable hairs. With such firm, sensitive, perifollicular nodules alternated hazelnut sized, sharply circumscribed, hairless, elevated areas of a spongy feel, arched like the surface covering of a superficial atheroma, of smooth and glossy aspect. Moreover, in irregularly outlined spots of fingernail to small coin size, there was an atrophic shrinkage of the scalp and a scarring destruction of the sebaceous glands. In such reddened retracted spots one saw the sparse hairs springing up from the network of skin furrows. Clinically and histologically the process showed many analogies to the initial forms of dermatitis papillaris

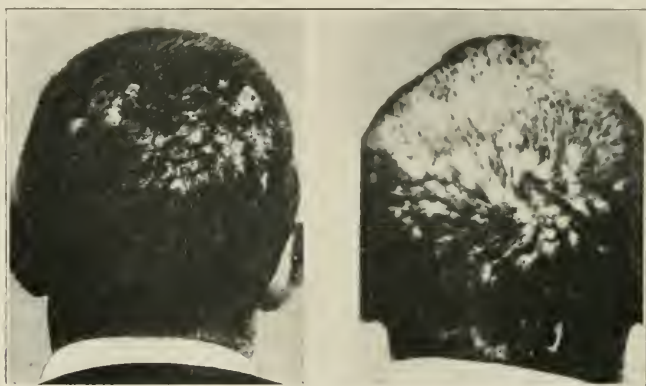


Fig. 2.—Author's case (left) and Ruete's case, showing the remarkable similarity between the two eruptions.

capillitii, without sharing its fate. The histologic preparations showed that here also there was a marked exudative perifolliculitis about the hair follicles and glandular adnexa. But while in the sclerosing folliculitis a proliferation and thickening of the cutaneous connective tissue was brought about through the inflammatory process, in the case under discussion the perifollicular infiltrate, formed principally of leukocytes, terminated in deep-seated abscesses, which after spontaneous rupture or operative opening left bald atrophic or thickened patches corresponding to their extent. Therefore, according to the anatomic findings, the process may be called a deep folliculitis causing baldness."

SPITZER'S CASE

Spitzer² recorded a case of "Dermatitis follicularis et perifollicularis conglobata (Lang)" which, beside the changes on the skin of the body

2. Spitzer: *Dermat. Ztschr.*, 1903, p. 109.

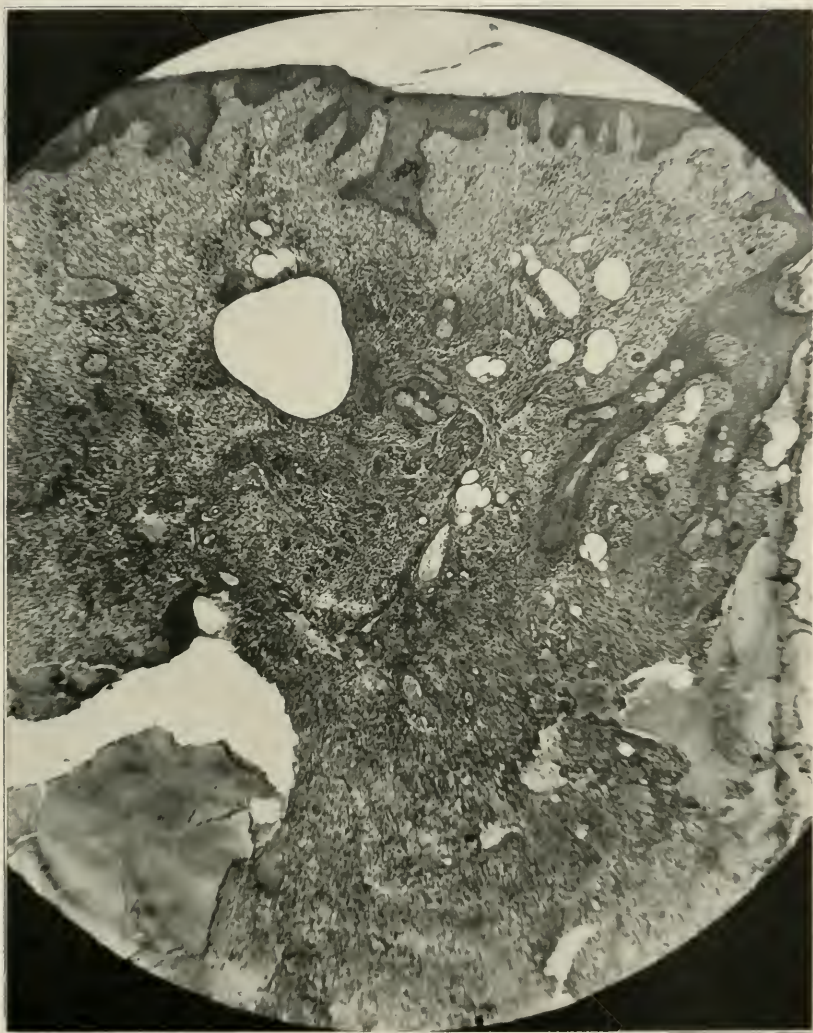


Fig. 3.—Low power; a general view. Infiltration occupying chiefly the middle and deep cutis; dilatation of lymph spaces and lymph vessels of the middle and upper portion of the corium; disintegration of the deep portions of the corium; dilatation and perivascular infiltration of vessels throughout the tissue.

described by Lang, showed a process on the scalp which was very similar to that obtaining in Ruete's case.

In this patient, a 24 year old weaver, there developed during his military service large, red nodules on the back, the size of lentils, which ruptured themselves and discharged pus. Later, similar nodules and abscesses appeared on the buttocks, the neck and the chest. In the course of a year he had to have more nodules opened in the axilla, on the nape of the neck and the occiput.

The patient, fully disrobed, presented a most striking appearance which cannot readily be illustrated here. All over the body of the otherwise well nourished patient, from head to toes, were a goodly number (about 100) of lesions, from millet seed to palm size, which could very well be followed in their evolution. They began as pinhead sized nodules of bluish-red color, some having comedones in their centers. In other lesions no comedones were to be found. Painless, notably without the signs of acute inflammation, they grew larger, and when they had reached about the size of a bean, were observed to break down internally. As a rule the skin was perforated in one or more places. In many areas, both on the trunk and on the extremities, the nodules becoming confluent, formed groups and presented the aspect of a smooth, bluish-red tumor which on pressure discharged pus from several often remote (peripheral) openings, an appearance reminding one of a turtle as it protrudes its legs from beneath its shell. Also on the trunk and in the axillæ there were countless scars, from the size of a millet seed to that of a dollar, at times blue-red at others white, with pigmented spots, in places resembling keloids, and in their serpiginous arrangement recalling gumma.

There was a different picture presented on the occiput and in the axillæ. In the first place the skin was unmistakably undermined, cavities dissected by the pus ramifying in all directions, bridged by thick swollen scars, forming a picture not unlike dermatitis papillaris of Kaposi. The introduced probe could reach far in all directions and emerged through an opening several centimeters away, which at first seemed to have no connection with the first. Similar, but not so marked, were the conditions in both axillæ.

For a searching histologic investigation Spitzer had unfortunately taken no nodules from the scalp, which would naturally have interested us most, but he obtained one bean sized nodule from the skin; this lesion fluctuated and had not ruptured. He found that the process originated from the follicle, that the neighborhood of the follicle showed inflammation and that granulation tissue had formed, reaching far into the connective tissue. By the advent of a bacterial infection as a secondary factor, suppuration resulted, with breaking up of the granulation tissue; extension of this process led to a deep disintegration and undermining of the subcutaneous tissue, terminating in extended, often keloidal scar formation.

RUETE'S CASE

Ruete's case is described as follows:

The patient was a man of 20 years. The parents and seven brothers and sisters were living and well. Three brothers and sisters had died in the first year of life from diseases of childhood. The patient himself had never been seriously sick. For three years he had had an acne of the face and back, sometimes better, sometimes worse, to which he had paid no special attention.

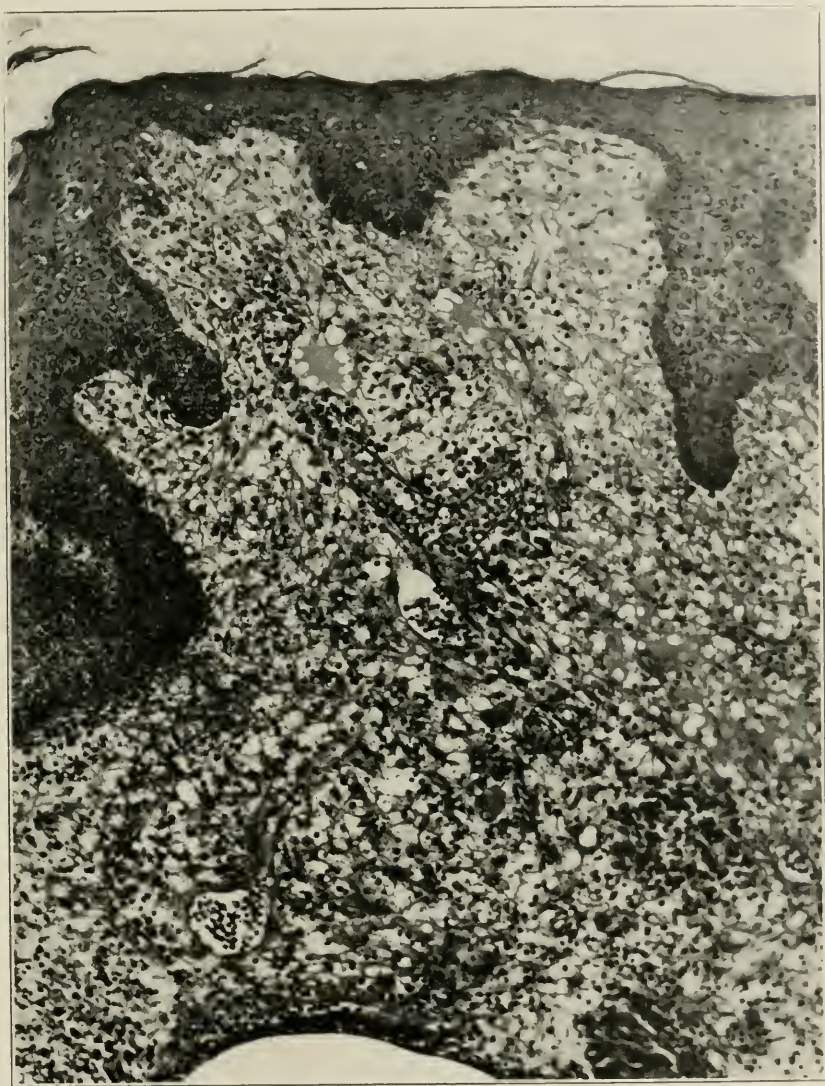


Fig. 4.—Medium low power; dilated lymph vessels filled with mononuclear leukocytes. The tissue is edematous and infiltrated with plasma cells and polymorphonuclear leukocytes. Below and to the right of one of the dilated lymph vessels are seen three or four swollen endothelial cells.

One year previously there had appeared on the middle of the scalp several small red "pocks," which had gradually enlarged and multiplied. A large portion of them suppurated, then ruptured and covered the scalp with thick crusts. The whole affected area was most painful on pressure. The patient was a medium sized, powerful man, well nourished, and his internal organs were free from evidence of disease. There was no general glandular enlargement. The urine was normal. On the back and chest were many acne pustules and comedones. There was a moderate acne of the face.

The scalp presented many yellowish-red to livid nodules ranging in size from very small nodules to walnut size lesions. On the tops of the nodules there were no hairs; in the spaces between them the hairs remained. They were not fixed firmly in the scalp but could be extracted by the slightest pull. Some of the nodules felt firm but most of them showed distinct fluctuation. Their site of predilection was the occiput; from the vertex the lesions extended in arches to the ears and below to the hair line; the hairs of the neck were not involved. Some of the nodules or abscesses were capped by little pustules. Most of the abscesses seemed to communicate with one another, and to have caused an undermining of the scalp; for if one pressed on a nodule on one side of the scalp, pus would be expelled from one on the opposite side; also the probe could be passed for 5 cm. under the scalp. In their course many abscesses ruptured spontaneously, and thus a large part of the scalp was bedecked with crusts and brownish-red scabs. The whole occiput presented a picture resembling a mountain range; lump rose above lump; a few rose strikingly over the level of the others. The rows of elevations were separated by deep depressions.

The picture is that of a perifolliculitis capitis abscedens et suffodiens. But other conditions have to be considered: a beginning folliculitis sclerositans and trichophytia profunda. Sporotrichosis must be ruled out. The patient remained under our care from Oct. 2, 1912, until Nov. 30, 1912, and was then discharged as cured.

The opened abscesses discharged a thick pus or a bloody serous fluid, and the leukocytic content was large. *Staphylococcus aureus* could readily be cultured from it; but the most careful implantations of glucose-agar and Sabouraud's medium and inoculations of rats failed to reveal the presence of them. The crusts having been removed, a 10 per cent. sulphur-zinc paste was applied, which, together with a course of autogenous vaccine injections and fractional roentgen-ray treatments totaling two units, brought about a speedy cure. The acne of the back and face quickly responded to a peeling paste.

For histologic examination a nodule about the size of a hazelnut was excised in such a way that sound tissue on either side of the lesion was included. It was fixed in alcohol and imbedded in paraffin. The sections were stained with hematoxylin-eosin, polychrome methylene blue, and van Gieson and Weigert's stains. For bacteria stains were made by Gram's method.

Microscopically there appeared at either side of the section almost normal skin, with well-formed rete pegs, hair follicles and glandular structures. As the middle of the section was approached, the papillae were obliterated, the follicles and glands were entirely lacking, and the

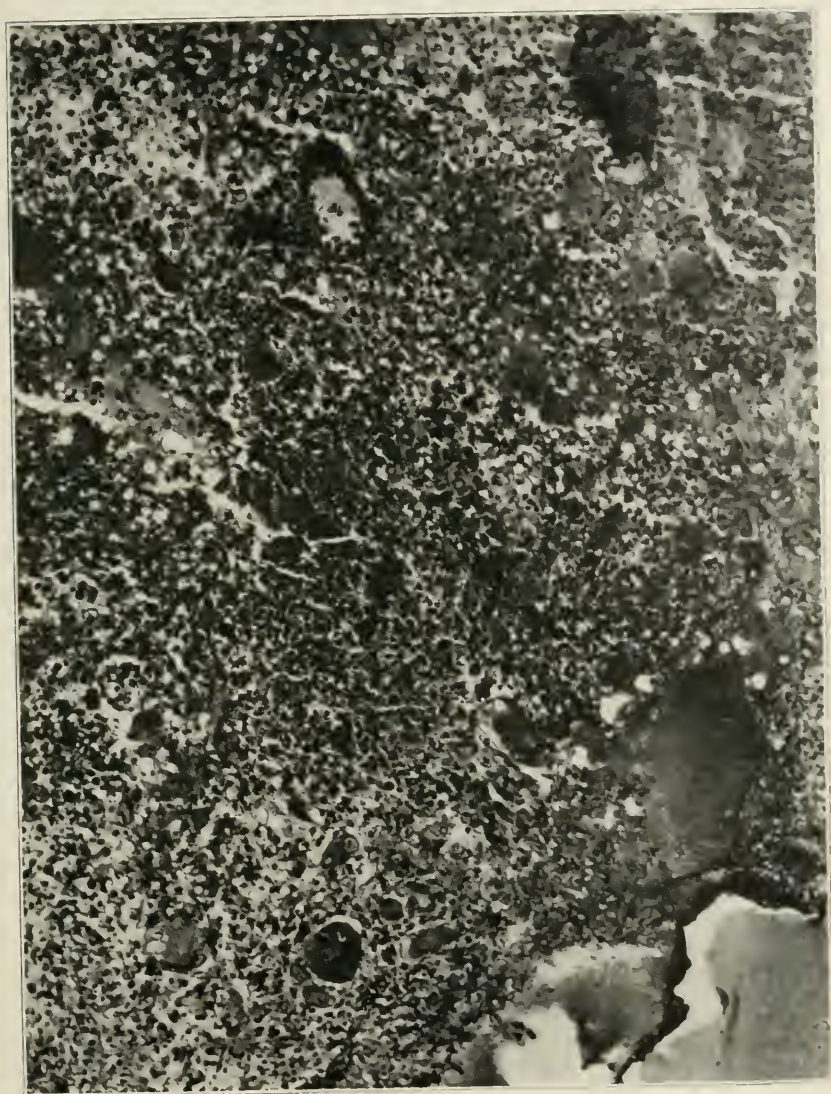


Fig. 5.—Low power; the polymorphism of the cellular infiltration and the breaking up of the collagenous tissue. See high power for cytology.

whole field was occupied by an apparently homogeneous, finely granular mass. The epidermis itself became thinner at the middle of the section, consisting of an ill-defined strip.

Under higher magnification, in the formerly apparently sound parts, there was a beginning small cell infiltration, especially in the perifollicular tissues. The hair was still in the follicle; but it was irregularly frayed out, and the papilla was occupied by a homogeneous, cell-free mass. The outer root sheath was partially destroyed and sparsely nucleated; here and there toward the periphery were collections of leukocytes which were a part of the infiltration that surrounded the follicle. This infiltration was composed partly of closely crowded mononuclear leukocytes. Since the leukocytes were found only in the outermost parts of the root sheath, while the inner parts were free, it was assumed that the pathologic process arose in the perifollicular tissues from which it then would invade the follicle itself. Therefore, the process was primarily a perifolliculitis, which terminated in a folliculitis.

The elastic fibers and the connective tissue bundles were still well preserved in this part of the preparation. But toward the middle of the section the latter were entirely lacking, in contradistinction to the conditions found in folliculitis sclerotisans nuchae, in which the involved region, with exuberant connective tissue growth, becomes sclerosed and eventuates in the well-known, almost board-like condition.

This part, on the whole, bespoke a fresh granulation tissue, with here and there a suggestion of tuberculous structure. As already noted, the epidermis was thinned to a few layers of rete cells. The papillary and subjacent regions were occupied by closely packed mononuclear leukocytes. There were many giant cells; several appeared in almost every field. Here and there one found the remains of glands and sparse remnants of elastic fibers which looked as though they had been torn apart and afterwards tied together, and were mostly tangled into knots. There was no normal connective tissue; but there were many capillaries within whose walls were countless polymorphonuclear leukocytes and eosinophil cells.

The Gram stain revealed goodly numbers of staphylococci in the follicles, in the perifollicular tissue and in the masses of granulation tissue. One cannot say whether these staphylococci were the primary agents of the disease, or whether they were later invaders that found a favorable soil in the inflamed skin.

SUMMARY OF CASES REVIEWED BY RUETE

Summing up the findings in these cases, Ruete finds "a singular and characteristic pathologic picture." It is "a severe affection of the



Fig. 6.—Low power; upper portion of cutis with dilated vessels containing polymorphonuclear leukocytes; perivascular infiltration of plasma cells and mononuclear cells, with edema of the connective tissue and some granular degeneration; dilatation of the lymphatics. Lower portion of cutis shows more infiltration with polymorphonuclear leukocytes.

occipital portion of the scalp, which consists in many large and small nodules, suppurating, becoming interconnected by burrowing, thereby undermining and excavating a large part of the scalp. They are hard to control by treatment, and leave, on healing, a flat, scarred alopecia in irregular spots, similar to that following psuedopélade."

In two of the four cases the process was not limited to the scalp, but was complicated, in one instance, by the presence of Lang's dermatitis follicularis et perifollicularis conglobata and in the other by acne vulgaris. It is suggested that these affections, preceding the occipital process, may perhaps be of interest etiologically.

The histologic examination indicated a disease process affecting the perifollicular tissue and the hair follicle, but which, unlike the folliculitis sclerotisans nuchae of Ehrmann, does not lead to a connective tissue proliferation. The resemblance to this disease is apparent in all the cases described as perifolliculitis capitis; but they cannot be identified with it, on account of a difference in pathology, which is evident histologically, and on account of the difference in the response to therapy of the two conditions. The other points in differential diagnosis have already been considered in the description of the cases, and it has been said that a fungus infection is to be ruled out by suitable laboratory methods. After the healing of the nodules and abscesses, the disease assumes an aspect which can easily be confused with the acné décalvante of Quinquaud. Also the pseudopélade of Brocq gives us approximately the same picture.

SIMILAR SKIN AFFECTIONS

Concerning acné décalvante, Boeck writes: "In the type described by Quinquaud the follicular changes assume various forms. Usually they are punctate pustules, like miliary abscesses, at first pinhead or even smaller, pierced centrally by an easily removable hair. The hair is soon destroyed and falls out spontaneously. It does not regrow, for the inflammatory process has produced an absolute atrophy of the hair follicle and its adnexa. The skin at the point attacked, after healing has occurred, is smooth, pale whitish, atrophic, thinned and depressed; it often shows the changes of scarring and might recall to a slight extent the scarring of favus. The hairless spots are irregular and of different sizes, but they do not usually attain dimensions which could be compared with those of pélade. They are scattered here and there over the skin with no tendency to unite in primary and secondary groups. Each little pustule is individual, and does not form a reddened, indurated, confluent mass, by coalescing with neighboring elements, as do the lesions of sycosis."

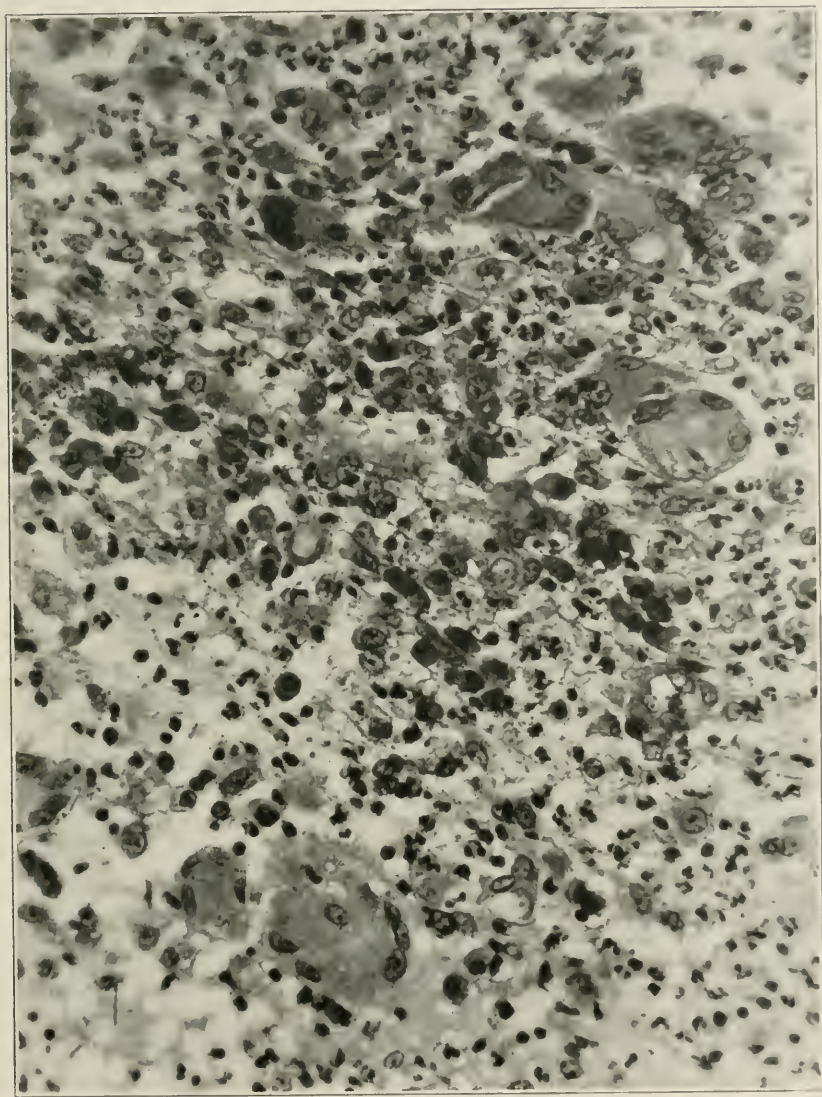


Fig. 7.—High power; types of cells: chorioplaques, giant cells, plasma cells, polymorphonuclear leukocytes, fibroblasts and round cells; degeneration of protoplasm of the chorioplaques; disintegration of the connective tissue.

The acné décalvante of Lailler and Robert is clinically identical with this form. But these authors state that after the first period, in which alopecia follows the acne-like pustules, the alopecia can extend further without being preceded by apparent acne pustules.

We have here, then, a picture which in its outcome is identical with ours. Here, as in our case, bald spots persist, whitish to pale-red in color, slightly atrophic, thinned, depressed and with slight scarring changes.³ Only in their beginning stages are the two forms entirely different. While Quinquaud's little primary pustules are pinhead size and smaller, and show no tendency to confluence, there is presented in our case a nearly opposite picture, with abscesses approaching walnut size, with a marked tendency to confluence, thus forming the above-mentioned peculiar picture of burrowing, and undermining the scalp.

An appearance very similar to that of the acné décalvante is presented by the pseudopélade of Brocq, with its many little bald spots occupying the vertex and the upper and middle portions of the occiput. These spots, too, are white or pale red, smooth and rather atrophic, of pinhead size and larger. They tend to become confluent, forming areas which enlarge as the disease progresses and approaching the size of the palm of the hand. The difference in the two diseases lies in the fact that pseudopélade progresses unheralded and that we never see suppuration of the follicles; at most one can now and then discern a slight reddening of the follicular mouth. There is, then, a marked difference in the mode of development of the two diseases, despite the fact that the end-results in both are about the same. At the beginning, perifolliculitis capitis resembles folliculitis sclerotisans nuchae which, however, has not this marked tendency to undermining and which, furthermore, does not share its ultimate fate, but nevertheless seems to form a connecting link between the two affections; it has much in common with both forms but cannot be identified with them.

The disease which Lang called dermatitis follicularis et perifollicularis conglobata is characterized (according to Spitzer) as a syndrome occurring only in persons with a coarse skin, with discrete, paired or grouped comedones, from which the pressure-atrophy comedone scars appear. One sees in the skin countless white, sinous or serpiginous depressions, which, if one is not familiar with the picture, would lead to the diagnosis of "artefact." The disease is characterized as a severe clinical syndrome, since the process may spread over a large part of the body surface, and since it causes deep destruction of the integument. Its nature is chronic and its course progressive.

3. For comparison, see the illustrations in Brocq's *Pratique dermatologique* 1:780.

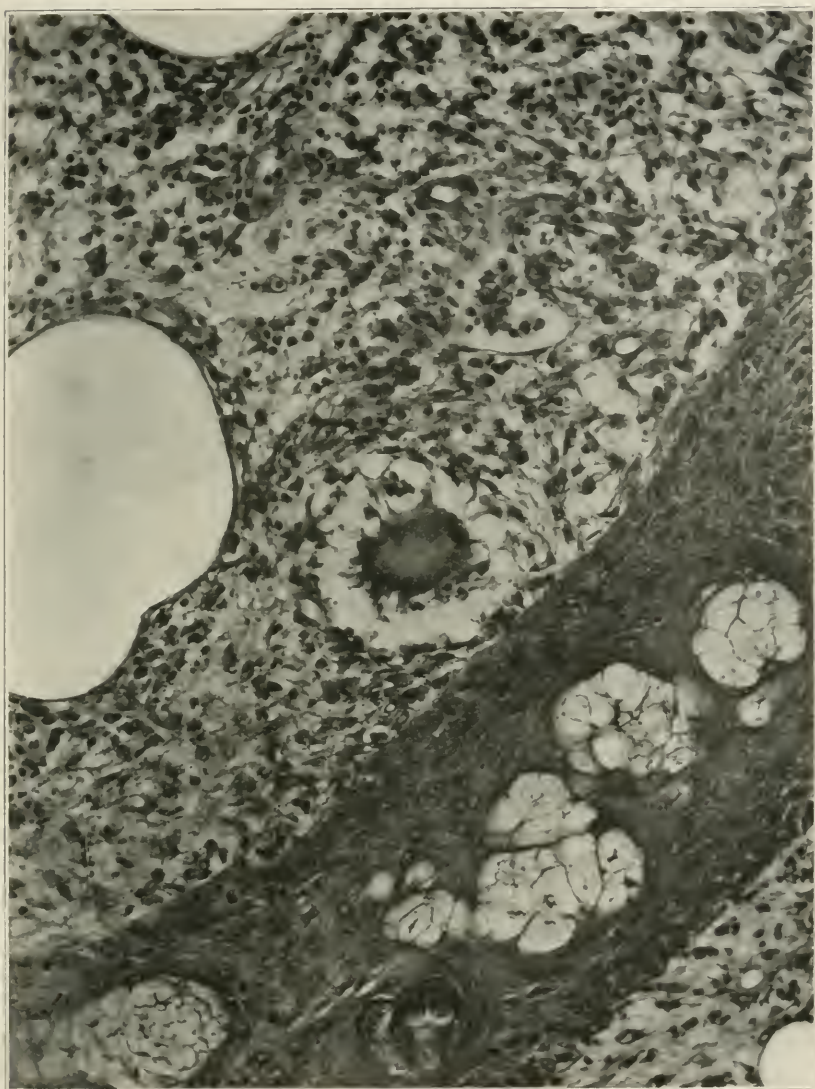


Fig. 8.—High power; an isolated chorioplaque within a lymphatic space, the latter containing a few small round cells; edema and degeneration of the surrounding tissue, together with a few plasma cells and many polymorphonuclear leukocytes.

Perifolliculitis capitis abscedens et suffodiens is probably a rare disease; for among the many cases of folliculitis and perifolliculitis appearing in the literature, Ruete was unable to find an example similar to his case; he also notes that the textbooks do not mention the condition. He is of the opinion that, as long as the etiology of the scarring alopecias is not better established, this affection should be classed as a separate entity.

A well defined example of this peculiar affection of the scalp recently came under our observation. The patient was referred for consultation by Dr. A. Monac-Lesser of New York, and we are indebted to him for permission to publish the following report.

REPORT OF CASE

History.—M. F., an unmarried man, aged 27, applied for advice on June 30, 1920. His family and personal histories were negative. His occupation was bookkeeping. He had always been in excellent health. His scalp affection began nine months prior to the consultation. He noticed the first lesion while he was serving with the A. E. F. in France. It began as a crop of what appeared to be ordinary pustules on the vertical portion of the scalp, accompanied with a little pain and discomfort. The army surgeon prescribed various antiseptic ointments, none of which effected an improvement, and the disease steadily progressed, so that in a short time, nearly the entire vertical portion of the scalp became involved in the process.

Examination.—At the time of examination, the diseased area occupied the entire vertical portion of the scalp, embracing an area roughly circular in shape, with a diameter of about 8 inches, the vertex of the skull forming the approximate center of the affected patch.

It was realized, at a glance, that the picture which confronted us was a most unusual one. Multiple furunculosis and folliculitis, pseudopélade, folliculitis décalvans, alopecia cicatrisata, and other similar diseases with which we are more or less familiar, could be readily ruled out, as the resemblance to these was at best only a remote one. In fact, it was chiefly the localization of the diseased area which brought to mind these different affections of the scalp.

The diseased area presented between forty and fifty more or less elevated hemispheric lesions, varying in size from that of a pea to that of a hazelnut. Some of these resembled ordinary soft, broken-down pustules and furuncles, free of hair, and emitting a seropurulent discharge; others had a more solid aspect, resembling sebaceous cysts. The larger lesions, however, presented a more striking appearance; they consisted of soft, flabby, hemispheric formations, which glistened as though coated with varnish, and which were distinctly opalescent in color; they reminded one of a partly collapsed green grape with its translucent skin. From some of these, a clear serous exudate could be expressed by merely touching the surface. Most of these lesions stood out prominently and separately; but here and there were areas which evidently resulted from the confluence of several individual formations. The surface of all lesions was free of hair, while in the spaces between them the hair remained but could be removed by slight traction. Many of these soft nodular lesions presented small openings, either at the summit or the base, through which a sticky fluid, serous and seropurulent in character would exude, bathing



Fig. 9.—Medium high power: a high grade edema of the connective tissue, and the plasma cell infiltration; polymorphonuclear cells scattered throughout the edematous collagen, and in the lymph spaces.

the surrounding area with a film of adherent exudate. Pressing a probe against one of these lesions would result in a forced extrusion of discharging matter from numerous sinuses situated from 1 to 3 inches away from the point of pressure. A probe could be passed into some of these sinuses, traversing the undermined scalp for distances varying between $\frac{1}{2}$ to 3 inches, toward the vertex of the skull. The introduction of a probe caused a moderate amount of pain. The other portions of the scalp were normal.

The various types of exudate were carefully examined, microscopically and culturally, by Dr. J. G. Hopkins, working in Prof. Zinsser's laboratory. There was no evidence of fungus or yeast infection. Smears revealed a great abundance of *Staphylococcus albus* and *S. aureus*, and streptococcus organisms. Sections and smears stained for tubercle bacilli were negative. The patient's Wassermann reaction was negative. He refused to submit to tuberculin and other tests.

Histopathology.—A section was obtained from a well formed nodular lesion, about the size of a pea. The tissue was stained with hematoxylin eosin, polychrome methylene blue, and Weigert's stain.

The striking feature of the case lies in the histopathologic structure of the excised lesion. This proved to be a pure granuloma and the presence of numerous giant cells pointed to a process suggestive of tuberculosis.

Low Power: The predominant feature consisted of a polymorphous cellular infiltration, occupying chiefly the mid and deep portion of the cutis; dilatation of lymph spaces and lymphatic vessels; edema of the entire tissue; dilatation of the blood vessels and perivascular infiltration throughout the tissue; and disintegration of the lower portion of the corium. Occupying the latter area, the infiltration was diffusely spread out, and the epidermis exhibited pressure atrophy and varying grades of acanthosis. There were many newly formed blood vessels in the upper and midcutis and greatly dilated lymph vessels resembling lymph sinuses.

High Power: Associated with the edema was a granular degeneration of the connective tissue. The infiltration was chiefly perivascular, for the greater part lying in the perivascular lymph spaces.

Cytology: The perivascular infiltration consisted chiefly of plasma cells, with outlying round cells. In the deeper portion, where the tissue was broken down, there were numerous giant cells, varying in shape and size, and in different stages of vacuolization; some of these might be called chorioplaques. Throughout the entire tissue, beside the cells enumerated, there were large collections of lymphocytes and polymorphonuclear leukocytes, without any special relation to vessels and lymphatics. Here and there isolated giant cells were located within lymphatic spaces. Within some of the dilated blood vessels there were many polymorphonuclear leukocytes and lymphocytes. The vessel walls were edematous, but there was no hyperplasia of the elements of the walls.

There was no distinct tubercle formation as is seen in sarcoid and lupus vulgaris; epithelioid and mast cells were not present.

COMMENT

The features of this case which are of interest to the dermatologist may be enumerated as follows: The disease is a rare one, only three examples being reported in the literature. The clinical appearances in these three cases are almost exactly alike. In its active stages, before

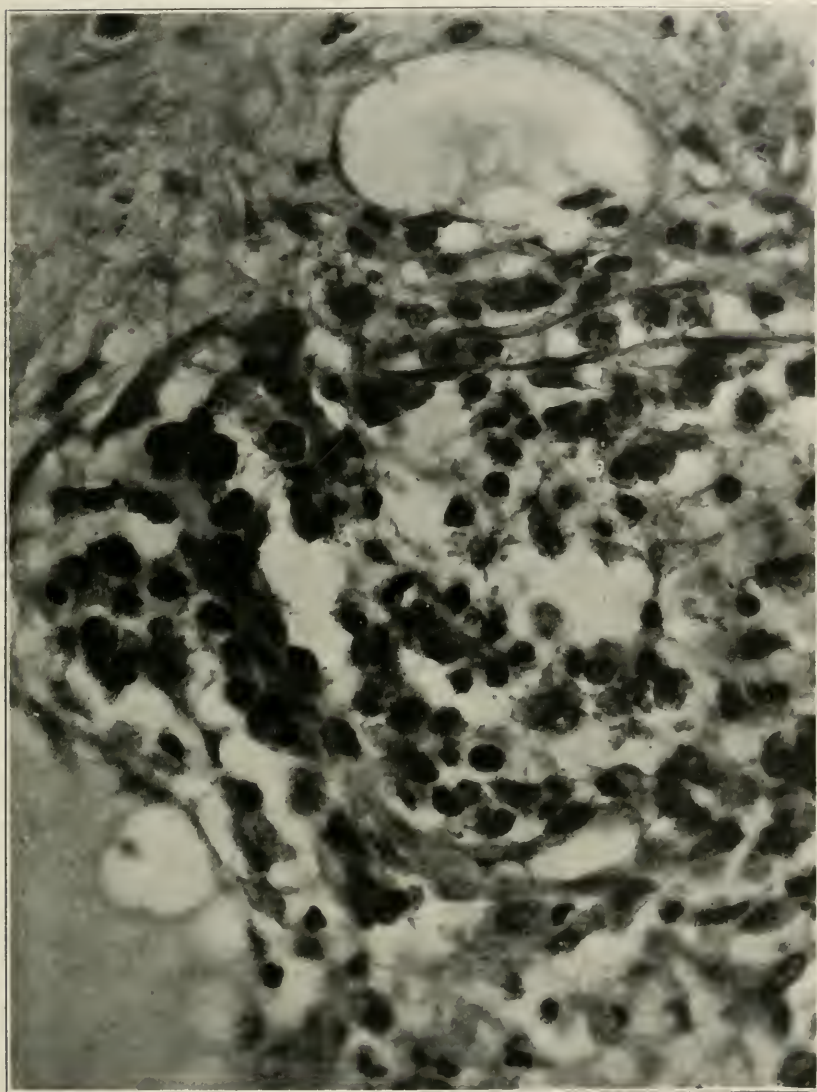


Fig. 10.—High power; the plasma cell perivascular infiltration; disintegration of the connective tissue.

atrophy and scarring have taken place, the disease picture differs markedly from that of any other atrophying and destructive disease of the scalp. In its end stages, after complete involution has occurred, the affected areas resemble those seen in folliculitis décalvans, pseudopélade and other similar conditions.

Assuming that the purulent element in this malady is due to secondary invasion of pus organisms, the causative factors are as obscure as in the destructive affections of the scalp mentioned before. This is of especial interest in view of the histopathologic structure of an active nodule, revealing, as it does, a granuloma, with features resembling a tuberculous process. An almost identical microscopic picture was seen in the case described by Ruete.

24 West Fifty-Ninth Street.

ABSTRACT OF DISCUSSION

DR. WILLIAM ALLEN PUSEY, Chicago: I have been looking for a description of this condition for more years than I am willing to admit. I had such a case when I was a dermatologic boy. I have seen no cases since and have not seen the cases in the literature that Dr. Wise has referred to. I am very much obliged to Dr. Wise for putting it on record in this country. My case was that of a neglected farmer's child, with a complete undermining of the scalp by a purulent infection. I conceived the condition at that time to be, and still consider it, multiple abscesses of the scalp, which coalesce under the thick fascia until the whole scalp is undermined. I should rather call it multiple abscesses of the scalp with destructive cellulitis. I enjoyed Dr. Wise's title, but I did not know what "suffodiens" meant and I would rather see the case put down by us and tabulated as multiple abscesses with destructive cellulitis of the scalp, than under a name that might confuse for a moment, at least, some of us.

DR. J. FRANK WALLIS, Washington, D. C.: In 1905 I reported a number of cases (ten) with clinical pictures corresponding closely to this one. The unusual picture and the ages, the eldest patient being about 20 or 21, did not at first suggest ringworm. Cultures and microscopic findings were negative until on close inspection a small black speck was obtained by pressing the pustules, and this contained a short hair stump with spores typical of the ringworm fungus. The cases were all in girls. For want of a name for this unusual condition I called it small multiple kerion. The clinical picture of the numerous abscesses undermining the scalp suggest the condition Dr. Wise has described.

DR. FRED WISE, New York: Dr. Pusey was right in interpreting the case as one of multiple abscesses, and we considered that when we looked at it, but there were two things against that diagnosis. The lesions were vesicular; they began as serous lesions, looking like a partially collapsed green grape, not like pustules which had ruptured. They began as vesicles, filled with clear serum and afterward became very much like impetigo. Another fact against a diagnosis of furunculosis is that furunculosis of the scalp is fairly common, whereas I think these cases with undermining are rare. Dr. Pusey said that he has seen only the one case, although I am sure he has seen much furunculosis of the scalp. In regard to Dr. Wallis' remarks, we examined the patient for kerion, although we did not expect to see kerion in an adult.

THE BOWEN TYPE OF EPITHELIOMA*

LOUIS B. MOUNT, M.D.

ALBANY, N. Y.

The early works on and workers in dermatology dealt with conditions in a more or less general way. There was to a certain extent an attempt, no matter how crude it may have been, to survey the field with a broad outlook, dividing it up here and there into by-ways. The development, enlargement and multiplication of these by-ways has progressed with such rapid strides that today there is an overabundance of paths which have no meeting place in common, or at best a blind ending. Synthesis is forgotten, while analysis is the password of the worker. Slight differences in clinical or microscopic appearances are made the basis of a new disease, with the result that a veritable maze of descriptions, under as great a wealth of titles, has arisen. Some of these titles are absolute misnomers, while others have no basis of fact justifying their usage.

An example of such usage is the word precancerous. This adjective should be banished from dermatologic nomenclature, for its employment is unscientific and unjustifiable. It is objectionable because it assumes something of which no one has any knowledge; it assumes the right to state definitely that such and such a lesion will eventuate in carcinoma. There is only one condition, among the large number placed in the precancerous category by Darier, for which the adjective might be used with any justification. This one condition is xeroderma pigmentosum, and even here the word cannot be made to apply to any definite lesion, but rather to the disease as a whole.

In 1912, Bowen¹ described two cases of chronic atypical epithelial proliferation. It is hard to understand why Darier² should have given the name *dermatose precanceruse de Bowen* to the dermatosis; for besides the objections previously mentioned, two of his own cases showed malignant lesions. Heimann³ aptly makes the statement that the term precancerous cannot reasonably be applied to conditions in which recognizable epithelioma exists.

And yet to Bowen⁴ the greatest credit is due for having first pointed out a dermatosis which had been either inaccurately interpreted

* Read at the Forty-Fourth Annual Session of the American Dermatological Society, Swampscott, Mass., June 2-4, 1921.

1. Bowen: J. Cutan. Dis. **30**:241, 1912.

2. Darier: Ann. de dermat. et syph. **5**:449, 1914.

3. Heimann: J. of Cancer Res. **1**:343 (July) 1916.

4. Bowen: J. Cutan. Dis. **33**:787, 1915.

previously, or not understood at all. Some of its manifestations were most often confounded with syphilis, and no doubt gave rise to those recorded cases of demonstrable syphilis which did not react to therapy.

A fairly complete survey of the literature has revealed the subjoined cases of this affection.

REPORT OF CASES

CASE 1 (Bowen).—A man, aged 49, in whom the disease first appeared nineteen years previous to examination as a good sized "pimple" on the gluteal region, presented, on the left buttock, an involved area, irregularly rounded, and measuring about 4 inches in diameter. It was covered with isolated and confluent lesions. The isolated lesions were represented by papules and tubercles slightly raised above the surface, flattened at their tops and generally rounded in their circumferences. They varied in size from one-eighth to one-half inch in diameter, and were usually situated at the outer borders of the patch. At the extreme they often took on an annular arrangement, or, in some instances, they formed almost serpiginous figures. A small amount of cicatricial tissue could be seen interspersed between the papules and the raised confluent areas.

The color of the lesions and patches was a dull red. The lesions were moderately firm but not hard to the touch. Their surfaces were somewhat uneven, with a papillomatous tendency in places, and here and there were scales and crusts, which were always extremely superficial.

CASE 2 (Bowen).—A man, aged 52, presented lesions which had existed for four or five years on the outer side of the calf of the right leg, forming an area resembling in a marked degree the lesions that have just been described as occurring on the buttocks in the previous case. The areas were from 3 to 4 inches in diameter and consisted of nodules from the size of a pinhead to that of a bean. Many were confluent, others discrete and well differentiated from the sound skin. They were raised about one eighth of an inch above the skin level and were flat on their surfaces. Many of the larger ones showed a papillomatous element. The color was a pale red. Some were covered with crusts, and a slight oozing occurred when these were removed. In some parts of the patches the lesions had joined to form irregular plaques and portions of rings.

CASE 3 (Darier).—A woman, aged 68, had had, for ten years, crusted plaques of an undetermined nature. Three cutaneous lesions in a state of activity were noted, together with a cicatrix:

1. On the left buttock there was a plaque of the size of the hand, polycyclic in contour, its edges made up of nummular brown crusts, its center cicatricial and of varied tints. The appearance was that of an ulcerated tubero-serpiginous syphiloderm. The crusts were formed of epidermic lamellae, infiltrated with dried serum, and beneath them was no sign of ulceration or pus, merely a red, eroded surface, smooth or slightly papillomatous in places.

2. On the anterior border of the right axilla, there was an oval plaque the size of a hen's egg, which had the appearance of a cornified papilloma, or a naevus verrucosus. Pieces of hyperkeratotic crusts could be detached from it with difficulty. This exposed a red, bleeding, sharply bounded surface. There was no induration of the underlying tissues.

3. The third lesion was situated on the right part of the back, at the level of the lower ribs, and represented an elevated tumor, of the form and dimensions of a macaroon, more than a centimeter in thickness, of a somewhat irregular surface, violet in color, and covered with a thin crust. It was of hard consistency and projected from an eroded, vegetating plaque. Corresponding to this tumor, there was an enlarged gland in the right axilla, firm and movable, of the size of a small walnut.

4. In the left groin there was a white cicatrix, produced by the excision of a former lesion, probably similar to the present plaques.

CASE 4 (Darier).—A woman, aged 39, reported that four years previously a warty patch had appeared on the inner aspect of her right ankle, and had slowly enlarged.

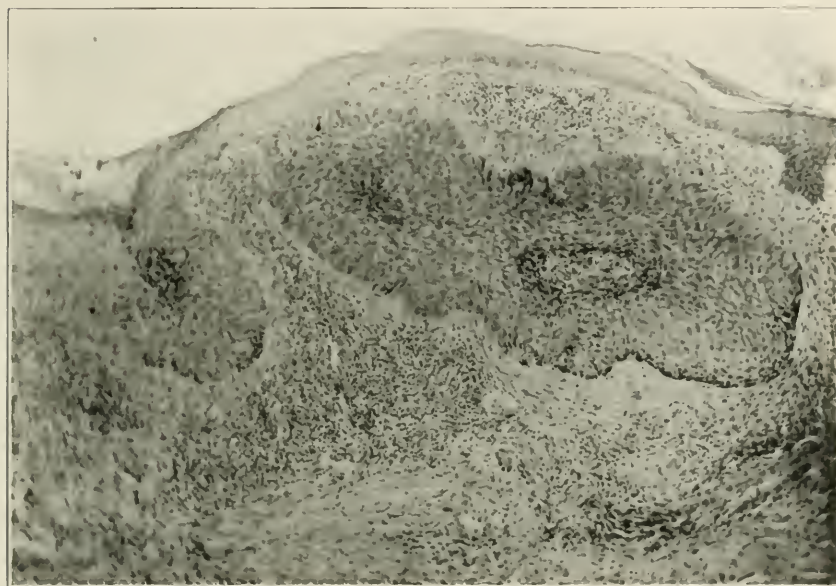


Fig. 1.—Photomicrograph of a section of a small nodule showing epithelial invasion suggesting tumor and adjoining inflammatory reaction.

On examination, a dozen lesions were found on her skin, varying greatly in appearance. The inner aspect of the right ankle was the seat of a plaque of irregular form and polycyclic contour, made up of an eroded central projection, which constituted a tumor, surrounded by more or less confluent, nummular papules.

The central tumor was formed of three lobes, was of the size of a small chestnut and was from 6 to 8 mm. in height. It was covered with a thin, adherent crust, beneath which was found a red, eroded, nonbleeding, somewhat irregular surface. It was of firm, almost hard, consistency.

The rest of the plaque was formed from the confluence of flat, discoid, papular elements, varying in size up to that of a fifty-centime piece. They were rounded, oval or square, sharply outlined, of firm consistency, with a smooth, flat surface, sometimes slightly scaling at the center.

There was no induration beneath this plaque, which was freely movable over the underlying tissues.

Three other varieties of lesions were noted:

1. There were red scaling patches, sharply circumscribed, flat, level with the normal skin and covered with fine white adherent scales. The skin was neither thickened nor indurated, but on the contrary seemed atrophic.

2. Yellow patches, oval and sharply bounded, covered with fine scales of the size of a fingernail, in which the skin appeared slightly atrophic, were found.

3. Finally, there was a brown spot on the back, without redness or desquamation, of the size of a two-franc piece, and sharply bounded.

There was no enlargement of the lymphatic glands.

CASE 5 (Darier-Danel).—A man, aged 63, exhibited the following lesions:

1. An oval ulcer of the forearm, granulating and bleeding freely, which had existed for six months, was situated on a large cicatricial surface.



Fig. 2.—Photomicrograph of another section of the same nodule showing true tumor formation, epithelial invasion and mitotic figures.

2. Papulosquamous lenticular lesions, with an infiltrated base, scattered over or grouped on this same cicatricial surface, which had existed for forty years, were noted. It was their recent transformation that had given rise to the ulcer.

3. There was an enlarged right axillary lymph gland. This gland later enlarged, broke down, and assumed the appearance of a rapidly progressive malignant tumor.

CASE 6 (Bowen-Pudor).—A man, aged 51, reported that skin lesions which began thirty years previously as a small papule on the chest, at the site of the present lesion of largest size, had gradually increased in size, and the numerous smaller lesions had gradually appeared subsequently. He had never been free from the affection since its beginning.

There were a dozen or more lesions scattered over the trunk, front and back. The largest and most conspicuous one was situated on the right side of the thorax, in the region of the nipple. It was an irregularly rounded plaque, 6 inches in diameter, scaling over most of its extent, superficial and sharply bounded. As a whole, it was only slightly reddened. The upper part had a distinct elevated rim, not wholly continuous, with ill defined papules, more or less confluent. This rim was of firm consistency, and the papules were somewhat whitish. The lower part of the patch represented a scaling, slightly atrophic surface, without perceptible induration. In the central portions of the patch, there were islands of superficial cicatricial tissue and atrophy, and scattered here and there over this cicatricial tissue and over the scaling surface were papules varying in size from that of a small pea to somewhat larger, of the same character and appearance as those described as constituting the upper margin of the lesion.

All the other lesions were mostly on the shoulders and back. They were of a papular and nodular character, varying in size from one quarter to one inch in their long diameter. Their shape was elongated or irregularly rounded, of a faint reddish color, and all were covered with a quite firmly adherent crust. They were slightly indurated and not surrounded with a hyperemic areola.

In the right axilla there were one or two slightly enlarged glands.

CASE 7 (Heimann).—A man, aged 56, for nine years had had an obstinate dermatosis on the right side of the neck, approximately over the mid area of the sternomastoid muscle. It resembled a crusted tuberoserpiginous syphilid, the convexity of which was emphasized by the presence of five or six scaling or crusted lesions, each a trifle smaller than a dime. They were dark brown, and removal of their covering revealed a proliferating area, moist with a serous secretion.

CASE 8 (Rasch⁵).—A woman, aged 50, had an epithelioma over the right temple, and over the right acromial region there was a granulated, reddish brown plaque, partly covered with thin scales. This had been present for ten years.

CASE 9 (Morrow and Lee⁶).—A woman, aged 50, whose condition was of nine years' duration, presented three types of lesions:

1. Numerous plaques varying in size from that of a pinhead to that of an adult palm, of a deep red color, occasionally tinged with yellow, oval or irregularly oval in outline, located on the anterior and posterior portions of the trunk were noted. Nearly all the plaques showed some scaling, and a moderate degree of infiltration to palpation. Crust formation now and then presented itself in the center or at the border of these lesions.

2. Nodules, firm to the touch, waxy in color, with a shining surface, were noted. Some of these presented telangiectases.

3. In the groin, about the umbilicus and on the scalp were fungating growths varying in size from that of an almond to that of a chicken egg. These were deep red in color, and bled freely at the slightest touch.

CASE 10 (Morrow and Lee).—A man, aged 52, had had the present affection for two years.

5. Rasch: *Hospitaltid.* **61**:1774, 1918.

6. Morrow and Lee: *J. Cutan. Dis.* **36**:1 (Jan.) 1918.

There were seven plaques on the shoulders and back, and a number of rodent-like nodules in the plaques, as well as at other positions independent of them. The plaques were oval, deep red in color, all with furfuraceous scales, sharp borders and no deep-seated infiltration. Some of the plaques showed faint cicatricial atrophy in the center.

CASE 11 (Korsbjerg⁷).—A man, aged 59, had had the disease for nine years. It began as a single spot on the side of the thorax. Since that time new lesions have appeared below the part first affected and have become attached thereto.

The involved area was about 10 by 11 cm., slightly raised, with brownish pigmentation outside of the actively affected area, and consisted of an upper and a lower portion.

The former had a polycyclic contour, bounded by a slightly raised zone consisting of round papular elements, varying in size from that of a pinhead to that of a hemp seed. These papules were pale red, flat and sharply defined, without a hyperemic halo, or white, firm and covered with thin, closely adherent scales mixed with serous exudate. Removal of the scales revealed a slight degree of moisture on an eroded pale red surface. Some of the papules had a central depression. The skin within the polycyclic border was pale red, without plainly marked cicatricial changes.

The lower affected portion, in its central part, was of the same character as the corresponding part of the upper. Its polycyclic border was broader and was formed of raised and projecting confluent papules which were round and flat-topped and covered with thick adherent moist, grayish-yellow scales. Removal of these scales revealed an eroded, dark red and moist surface. Infiltration was present to a slight degree, but the portion attacked was not adherent to the underlying tissue.

No swelling of the regional lymph glands was demonstrable.

The white blood cell count was normal; and the complement-fixation test for syphilis was negative on two occasions.

CONCLUSIONS

From the foregoing cases, these facts can be deduced:

The condition is extremely chronic and progressive, varying in duration from two years (Case 10) to forty years (Case 5). It occurs in both sexes at varying ages, the youngest being 39 (Case 4), the oldest 68 (Case 3). There is no site of predilection, either the trunk or extremities or both being involved. The primary lesion is a small papule, firm to the touch and slightly elevated. Its surface may be flat with or without a central depression. The papule is either pale red, deep red, or skin colored with no congestive halo in the periphery. Later these increase in size, become scaly or crusty, remain discrete or become confluent or grouped. As a result of these changes in size and arrangement, three types of lesions are formed; nodules, plaques and fungating growths. These have been so amply described in the foregoing review of cases that their definition again would be repetition.

7. Korsbjerg: Hospitalstid, 62:1233 (Nov. 5) 1919.

The histologic findings in these cases were more or less uniformly the same.

The corneus layer showed a varying degree of hyperkeratosis with some parakeratosis. Imperfectly cornified cells of the type of the "corps ronds" described by Darier were at times found. The granular layer was wanting in places. In the rete, there was a marked proliferation, with a pronounced intracellular edema. Karyokinesis and amitoses with a peculiar clumping of the nuclei and vacuolizing of the cells was evident. This was most marked in the upper layers. The inter-papillary pegs were hypertrophied, plump at places, and reaching separately into the corium; but in most places they formed compact epithelial masses.

A layer of typical palisade cells usually formed the boundary between the corium and overlying epithelial structure, but here and there cells of varying sizes were found.

The changes in the corium were constant, consisting of a dilatation of the superficial capillaries, which were surrounded by a more or less dense cellular infiltration composed of plasma cells with round cells and a few polymorphonuclear leukocytes. An interesting finding in this connection was that the older the lesions were, the less plasma cells and the more round cells were seen. In addition to the microscopic departure from the normal mentioned before, Cases 3, 5, 6, 8, 9 and 10 showed, in one or more lesions, manifest carcinomatous changes.

The review of this subject was occasioned by the subjoined case.

A woman, aged 41, of medium stature and weight, whose family and past history revealed nothing of importance, presented a dermatologic condition which had begun eight years before, with the appearance of a small spot on the back of her left hand. Since that time there has been a gradual increase in the number of these spots. Examination disclosed, scattered over the arms, face, neck, upper part of the chest and back, a multiplicity of lesions. There were papules, varying in size from that of a pinhead to that of a split pea, of either skin color, or pale or deep red. Some of them presented an uneven surface, while others were flat-topped, with an occasional depression. Larger, slightly elevated scaling areas of a deep red color and about the size of a dime could be seen. Here and there were crusted nodules which, on the removal of the crusts, disclosed an eroded, serous surface. Another type of lesion consisted of a delicate, slightly raised, more or less perfect ring, made up of minute papules enclosing a reddened slightly scaling area. These lesions were about three quarters of an inch in diameter.

The largest involved area was on the shoulder and consisted of a red plaque, irregularly rounded, and about 1½ inches in diameter. This plaque had a slightly scaling centrum, with crusts here and there. The crusts and scales were easily removed, and disclosed a moist red base. The periphery of the patch had an irregular outline of dull red papules, giving a clinical picture much like that of a syphiloderm.

The blood cell count, both white and red, as well as the hemoglobin estimation, was normal. The Wassermann reaction was negative, and nothing abnormal was found in the urine.

Unfortunately, before the patient's hasty departure, no photographs and only one biopsy could be obtained. This biopsy, consisting of one of the small nodules, revealed an epithelioma, basocellular in character. Had it been possible to examine a section of the plaque on the shoulder, the findings undoubtedly would have been the same as that in the other recorded instances.

Even in those cases in which a complete histologic picture of carcinoma could not be found, the changes were highly suggestive of such a growth, in fact, so suggestive that I feel that the dermatosis in question is carcinomatous from the start. This same opinion is voiced by Morrow and Lee in their statement that "Since the plaque is but one variety of the clinical types of the affection and as the other types are characteristically epitheliomatous, it seems best, for the present at least, to class the malady under the name of 'Bowen's type of epithelioma.'"

ABSTRACT OF DISCUSSION

DR. JOHN A. FORDYCE, New York: I fail to see any justification for objecting to the use of the term "pre-epitheliomatous." It is a word which is in common use, and it certainly expresses something that cannot be expressed in any other way. We have keratosis from light, from arsenic and other things, and any of them is different from the normal skin. It seems to me that we are entirely justified in using that term, not only from what we see, but because of its general use. What other term could we use for expressing the predisposition of the skin to epithelioma?

DR. WILLIAM ALLEN PUSEY, Chicago: Had Dr. Fordyce not beat me to it, I would have made the same criticism. The conditions Dr. Fordyce mentioned are all pre-epitheliomatous. When we apply that term we do not mean that a lesion will certainly turn out to be an epithelioma, but that it is a condition which is often followed by epithelioma. A pre-nuptial engagement may not be followed by marriage, but it very frequently is. These growths certainly are not always followed by cancer, but frequently they are, and precancerous is a perfectly accurate term to apply to them.

DR. RICHARD L. SUTTON, Kansas City, Mo.: Some years ago, I had under observation a case which I had diagnosed as multiple basal-cell carcinoma of the skin. The lesions, about a dozen in number, were confined to the dorsal surface of the trunk.

Some were not keratotic, but the majority were, and several were frankly carcinomatous (as shown by biopsy). The patient was under observation for several months, and the lesions appeared to pass through a certain distinct cycle, and ultimately became cancerous. Dr. Howard Morrow, while at my office one day, saw the case, and called my attention to its identity with the disorder originally described by Bowen. I think the term "precancerous" should be retained for lesions of this type, as well as for the designation of certain other keratoses, the majority of which finally become malignant.

DR. AUGUST RAVOGLI, Cincinnati: At the clinical demonstration, a woman with a small epithelioma at the temporal region was shown. It could not be called an epithelioma, but the condition could be called pre-epitheliomatous or precancerous. I do not see the reason why the term precancerous should be abolished. I think it is a correct term, because when an epithelioma starts, it

starts always on a keratotic patch, which we often find in the skin on the face, in the grooves around the neck at the edge of the hair and in the eyebrows. When we see a section of the epithelioma, we see the different types according to the point from which the epithelial cells start to go into the connective tissues of the derma. Sometimes we see that they come from the follicles of the hair, and also from the sebaceous glands, and then they spread, constituting what has been called the follicular epithelioma. We have others which start directly from the corium. I believe precancerous conditions have to be treated in the same way as epitheliomas.

Regarding what Dr. Mount said about the plasma cells, in my opinion they are nothing but an effort of nature to save the surrounding tissues from the spread of the epithelial cells which constitute the cause of the dreadful disease.

DR. HAROLD N. COLE, Cleveland: I should like to say that I agree with Dr. Morrow that the disease is not so rare as it has been considered. Just now I have three cases under treatment, and I shall be glad to try out his suggestion.

This may savor somewhat of heresy, but I should like to hear some of the older men say what they think of the pre-epithelioma of Paget's disease. We have two divisions of opinion, one of which considers Paget's disease an epithelioma from the beginning, and the other which considers it a type of eczema, which later becomes epithelioma. Is the same not true with Bowen's disease? In many ways they are certainly very much alike.

DR. SIGMUND POLLITZER, New York: At a recent meeting of the Academy of Medicine in New York, the subject of epithelioma of the skin was discussed. At that meeting this very question of the term "precancerous" arose, and I made the points which Dr. Fordyce has made this evening. I think a very cogent reason for the retention of the term precancerous is founded in the circumstance that it calls attention to the fact that certain types of dermatoses frequently become cancerous, and thus puts physicians on their guard. I am strongly in favor of the retention of that term.

As to the relation of Bowen's disease and Paget's disease, that has been much discussed, but clinically the two conditions are very different. That the difference is not simply due to differences in location is apparent from the fact that, in Paget's disease of the scrotum and adjoining regions, the appearances are not at all like the epithelioma of Bowen. Histologically, there is a considerable resemblance between the two diseases, especially in the large number of dyskeratotic figures in the tissues and the vacuolization that is so characteristic in Paget's disease. The two diseases, however, are clinically so different that I should hesitate to group them together.

DR. LOUIS B. MOUNT, Albany: I have nothing to add to the paper, but should like to have you see the Lumiere plate, which Dr. Morrow brought along, showing an example of this condition.

DR. HOWARD MORROW, San Francisco: I think these cases are not nearly so rare as we thought they were several years ago. Since reporting on these cases four or five years ago, I have seen on an average of one case a year.

In answer to Dr. Pusey, the nodules of the Bowen type are indistinguishable microscopically from rodent nodules. They all have a small, rolled border, often so small as to be scarcely visible to the naked eye; but when the skin is stretched, the border is always visible.

About the treatment, I think possibly the best treatment is to curet the nodular plaque and then apply any form of caustic acid. There is very seldom recurrence after such treatment.

THE TREATMENT OF LATE SYPHILIS, AND OF SYPHILIS IN MOTHER AND CHILD

A RÉSUMÉ OF PRINCIPLES *

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The problem of the treatment of late syphilis differs in essential particulars from that of early or of true asymptomatic (latent) syphilis. In early syphilis we are still, in spite of the disturbing revelations of Warthin,¹ of Brown and Pearce,² and of Eberson,³ striving for radical cure of the infection. In the late stages of the disease, the problem becomes one of symptomatic improvement and arrest. The early infection usually involves the unimpaired human body. In the late years of the infection the physiologic changes of advancing years are added to the disabilities produced by the action of the disease on vital structures. The characteristic reaction of the body to the syphilitic infection opposes another obstacle to treatment. The slowly progressive fibrosis walls off the organism from the carriers of remedial agents, the blood and lymph. By the induced obliterative endarteritis, the accessibility of foci to spirocheticides injected into the blood or distributed by it is probably materially reduced. In the slowly progressing or latent infection there must also exist a balance between the offensive powers of the organism and the defensive powers of the host. If the organism could be confined within the infected individual and this balance be perfectly maintained, the commensalism would serve all the purposes of the radical treatment methods of the "extirpators." The large majority of late syphilitics have probably effected some measure of compromise with the spirochetal invader, and judgment must be exercised in the disturbance of this relation.

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

1. Warthin, A. S.: The Persistence of Active Lesions and Spirochetes in the Tissues of Clinically Inactive or "Cured" Syphilis, *Am. J. M. Sc.* **152**:508 (Oct.) 1918; New Pathology of Syphilis, *Am. J. Syphilis* **2**:425 (July) 1918.

2. Brown, W. H., and Pearce, Louise: A Note on the Dissemination of *Spirochaeta Pallida* from the Primary Focus of Infection, *Arch. Dermat. & Syph.* **2**:470 (Oct.) 1920; Syphilitic Infection of the Central Nervous System of the Rabbit, *Ibid.* **2**:635 (Nov.) 1920.

3. Eberson, F.: Dissemination of *Spirochaeta Pallida* in Experimental Syphilis, *Arch. Dermat. and Syph.* **3**:111 (Feb.) 1921; Eberson, F., and Engman, M. F.: An Experimental Study of the Latent Syphilitic as a Carrier, *J. A. M. A.* **76**:160 (Jan. 15) 1921.

APPRAISAL OF POSSIBILITIES AND THERAPEUTIC DECISIONS

The aim of treatment in late syphilis is to carry the infected individual through the fullness of his years, with maximum attainable efficiency and minimum danger to his contacts and to the social order. The first step in the treatment of late syphilis is an appraisal of possibilities, including:

1. An estimate of life expectancy based on age, on damage already done, on the supposed activity and rate of progress of the process, and on its probable refractoriness to treatment.

2. An estimate of the handicaps imposed by complications not directly due to syphilis, such as tuberculosis, nonsyphilitic mental disease, hypertension, chronic interstitial nephritis, diabetes, and so forth.

3. An estimate of the tolerance of the patient for the various methods of treatment available.

4. An estimate of the probable response to treatment of the most vital structures involved.

Treat late syphilis by the indications in vital structures and not in structures nonessential to life. Only a searching examination of the entire body can provide the information for such an appraisal. While the milder forms of treatment may be begun, arsphenamin should seldom be administered until this appraisal is reasonably complete. The inherent crudity of our methods of estimating the condition of many important structures must be remembered and allowed for in making the estimates mentioned. Particularly in involvements of the vascular system is this caution important.

The Herxheimer reaction is as much a feature of late syphilis as of the acute infection. It must never be lost sight of, and the possibility that it will have serious effects, either from the location of the involved structure, as in the case of the larynx or a cerebral vessel, or from its functional importance, as in the case of the myocardium, must be carefully weighed. In general, it is conservative to give all individuals affected with late syphilis mercurial preparation.

The control of infectiousness in late syphilis, while traditionally of little import, deserves more consideration, in the light of recent work on carriers,⁴ especially in the woman who is pregnant or may become pregnant, or in the potential father of children. It is, I believe, a good rule that late cases deserve nearly as much arsphenamin as early cases, for the control of this aspect under the limitations imposed by the preliminary survey and the progress of the case.

Adjustments required by the process of healing are factors in therapeutic decisions in late syphilis. When healing begins under treat-

4. Footnote 3, second reference.

ment, the attempt made by the body to compensate for a pathologic change is disturbed, made to take another direction. An adjustment to the effects of cicatricial contracture as well as to the Herxheimer reaction must be made, at times with a paradoxical increase in symptoms, as pointed out by Wile,⁵ for syphilitic hepatic cirrhosis. Cicatricial stenosis of the esophagus and rectum, even of the hour-glass stomach, occurs. I am inclined to believe that, so far as the heart is concerned, acute myocardial ischemia, anginal attacks of increased severity, even the development of certain physical signs of aortitis and aneurysm, may be the results of too energetic treatment and too rapid healing.⁶

In the complete appraisal of a case, consideration should be given to the vasculotoxicity of arsphenamin,⁷ its hepatotoxicity,⁸ and the seriousness of cutaneous exfoliative accidents. At first a theoretic consideration, these items have acquired a very real meaning in my experience with late syphilis. The relatively low toxicity of arsphenamin for the kidney makes it a serviceable drug in nephritis, but there is a notable exception. In low renal function from back pressure, and in pyelonephritis, often a complication of neurosyphilis, it must be used with caution. The history of previous dermatitis as a relative contraindication to arsphenamin does not receive the attention it deserves.

The renotropism of mercury, its ability, by certain modes of administration, to increase the cutaneous reactivity to arsphenamin, its depressant action when overdone and the unfavorable effect on severe

5. Wile, U. J.: Syphilis of the Liver, *Arch. Dermat. & Syph.* **1**:139 (Feb.) 1920.

6. I was interested to find Hubert (*Zur Klinik und Behandlung der Aortensyphilis*, *Deutsch. Arch. f. klin. Med.* **128**:317, 1919) in accord with me on this point.

7. An interesting suggestion that cardiac dilatation after arsphenamin is due to increased pulmonary pressure produced by the obstruction of the circulation or vasoconstriction, and is dependent on the alkalinity of the preparation is made by Smith (*Further Pharmacologic Studies on Arsphenamine*, *J. Pharmacol. & Exper. Therap.* **15**:279 [June] 1920). This combined with the observation that neo-arsphenamin is not precipitated in the blood (Schamberg, Kolmer, Raiziss and Weiss: *Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin*, *Arch. Dermat. & Syph.* **1**:235 [March] 1920) would seem to suggest the desirability of neo-arsphenamin in cardiac syphilis.

8. The numerous recent articles on jaundice as a complication due to the toxic action of arsphenamin are reviewed from the standpoint of a possible infectious factor in Stokes, Ruedemann and Lemon's paper (*Epidemic Infectious Jaundice and its Relation to the Therapy of Syphilis*, *Arch. Int. Med.* **26**:52 [Nov.] 1920. Milian continues his vigorous defense of treatment (*Jaundice and Arsphenamin*, *Médecine*, Paris, **2**:113, 1920; abstr., *J. A. M. A.* **76**:143 [Jan. 8] 1921). Compare also Hallam (*Post-Salvarsan Jaundice*, *Lancet* **1**:1356 [June 26] 1920).

anemias, described by Foucar and myself,⁹ are among the principal points to be considered. The old-time bugbears of stomatitis, salivation, and gastro-intestinal disturbance have been reduced to relative insignificance by dental prophylaxis, diet, and intelligence in dosage.

As in its resistance to the disease itself the body shows a generous margin of safety, notwithstanding the effect of prolonged or massive treatment, so no symptoms or good recoveries may result from the most flagrant abuse of both arsenic and mercury. But I have always felt that the avoidance rather than the correction of toxic or debilitating effects is the ideal, and to that end have insisted on a number of precautions against complications, which in the end, I believe, protect patients from the small but cumulative insults which too often keep them in a substandard condition under intensive treatment, even though the individual by-effect may not become conspicuous in itself. In late syphilis, in which the margin between treatment requirements and treatment tolerance is often very small, such protective measures may make all the difference between success and failure. In the nine cardinal rules for the management of the excretory mechanism which I shall quote here from my discussion of this point before the Institute for Venereal Disease Control, I should mention that the emphasis on microscopic blood as an evidence of renal damage is drawn from an unpublished study, by Wilder and myself, of the effect of prolonged intensive treatment for syphilis on the kidney. I want also to direct attention to the influence of the atonic bladder with retention symptoms in retarding the progress of patients who would otherwise do well. I am satisfied that the terminal picture in more than one practically arrested but none the less fatal case of neurosyphilis is a composite of depressed renal function and ascending infection of the urinary tract.

MANAGEMENT OF THE EXCRETORY MECHANISM

1. A cathartic should be given after each arsphenamin injection, and a mild laxative during the course.
2. A weekly urine examination should be the rule.
3. Special attention should be paid to (*a*) casts, (*b*) red blood cells, and (*c*) pus in the urine (catheterized in women).
4. Many or persistent casts mean renal irritation. Occasional showers are not significant.
5. Red blood cells of renal origin mean renal injury.
6. Pus or blood of vesical origin may be an index of cystitis due to urinary retention. In neurosyphilitics with pyuria search should be

9. Foucar, H. O., and Stokes, J. H.: The Effect of Treatment for Syphilis on Severe Anemias, *Am. J. M. Sc.* to be published.

made for atonic or "cord" bladder with residual urine, secondary cystitis and pyelonephritis, rising blood urea, and falling phenolsulphonephthalein excretion.

7. The excretory mechanism should be protected by (a) extirpation of focal infections, (b) administration of fluids and alkaline diuretics (*potus imperialis*), (c) catheterization and irrigation of neurogenous bladders, (d) diet regulation (low proteins), and (e) suspension or moderation of treatment if other measures fail.

8. The physician should not discharge a neurosyphilitic patient without being satisfied with regard to his renal function, his blood urea content, and the integrity of his bladder mechanism.

9. Every tabetic patient should be regarded as potentially uremic.

FACTORS IN A SUCCESSFUL THERAPY

Schamberg, in a personal communication, has suggested that the simultaneous administration of arsphenamin and mercury results in the retention of the arsenic with increased risk of exfoliative accidents.¹⁰ That this retention is so serious as to justify abandoning the simultaneous use of the two drugs I have not as yet been able to convince myself from clinical evidence. Exfoliative accidents in my service come in waves, and have had what seemed to be more than a casual relation to intercurrent and focal infection.

The "broken immunity" of arsphenamin-treated early syphilis, long familiar in clinical experience and now experimentally verified by Brown and Pearce,¹¹ has, I believe, occasional homologs in late syphilis.¹² All of you have no doubt seen the marked acceleration of the unfavorable progress of some cases of neurosyphilis following arsphenamin, scarcely explainable as mere arsenic fastness. I believe it is a conservative practice never to terminate a period of treatment with arsphenamin, but to finish with mercury, if it be only by mouth.

In early syphilis, symptoms have little meaning as therapeutic guides; in late syphilis they may be supremely important; in fact, their disappearance may be the sole criterion of successful therapy. Eighty-five

10. Klauder, J. V., and Kolmer, J. A.: The Urine in Syphilis. Report of Laboratory Studies, Including the Wassermann Reaction, in Sixty Cases, J. A. M. A. **76**:102 (Jan. 8) 1921.

11. Brown, W. H., and Pearce, Louise: The Resistance (or Immunity) Developed by the Reaction to Syphilitic Infection and Some of the Effects of the Suppression of this Reaction, Arch. Dermat. & Syph. **2**:675 (Dec.) 1920.

12. The unfavorable effect of minute dosage is discussed by Bronfenbrenner, J., and Schlesinger, M. J.: Generalized Infection in Syphilitic Rabbits Resulting from the Inadequate Salvarsan Therapy, Proc. Soc. Exper. Biol. & Med. **18**:94, 1920.

per cent. of late syphilitics, in our experience, selected with only a reasonable degree of discrimination as to therapeutic outlook, should undergo symptomatic arrest and be ultimately placeable on observation.¹³ One is occasionally disconcerted by the symptomatic Herxheimer flare-up which dominates the picture during the first three or four weeks of a moderately intensive course. The changes in the Wassermann reaction, while of interest, are not the sole evidence of the efficacy of a method of treatment, and are in fact at times not even an important consideration. In general, a persistent positive reaction is a signal for a rechecking of the fundamental examination and appraisal of the case, and a Wassermann relapse calls for more treatment in the absence of contraindications.

A legitimate distinction should be drawn, in estimating the progress of late syphilis under treatment, between scars and evidences of activity. It is a matter of little moment that a tabetic patient does not recover his knee jerks or a patient with cardiac disease get rid of his aortic murmur. On the other hand, it is decidedly in point if anginal attacks increase in frequency in coronary sclerosis, or if a patient with diffuse hepatitis has a recurrence of jaundice, or the liver fails to decrease in size. Paradoxical pictures at times occur, in which the signs representing scars become more conspicuous as the symptoms representing functional impairment disappear. Ascites developing in hepatic cirrhosis under treatment,⁵ bone sequestrums discharged through a sinus, atrophy of the optic nerve as a marked neuroretinitis involutes, pulsation in an aneurysm as the periaortitis subsides, are examples in point. Failure of structural improvement to occur even with marked symptomatic improvement is familiar enough in aneurysm and gastric syphilis. Functional improvement may also outstrip all expectations based on the recognized structural change, particularly in inflammatory processes. In the eye and ear, gains in sight and hearing sometimes have a qualitative rather than quantitative character and may again exceed all expectations.

How far shall treatment be carried after the disappearance of symptoms when the signs are not such as to furnish a guide to the progress of the case? In general, I should say to the point of giving as much treatment as in an early case, provided tolerance permits. This is a vital proviso. The abuse of a patient's tolerance of treatment in late syphilis even more than in early syphilis is, I believe, a serious error, since it is impossible to predict that the course of his infection may not be such that he will be under treatment at intervals all his life. On the

13. Stokes, J. H., and Busman, G. J.: A Clinical study of Wassermann-Fast Syphilis, with Special Reference to Prognosis and Treatment, *Am. J. M. Sc.* **160**:658 (Nov.) 1920.

other hand, timidity in using effective measures may be precisely the thing which projects the patient onto the other horn of the dilemma. It is for these reasons that I lay much stress on the use of every available means in late syphilis to improve the general status of the patient and to protect him specifically from therapeutic by-effects. When objective guides to the effect of treatment exist, I have found it well to persist beyond the first negative finding, so as to prevent relapse. The question as to whether relapse can be indefinitely postponed by this means remains as yet unsettled. In general, I prefer mercury for the supporter of the resistance that prevents relapse, but I have seldom felt it necessary to urge the life-long "forty rubs a year" if the patient would consent to periodic complete examination. Dismissal of the patient with any such blanket directions seems to me to lay him open to all the uncertainties of an infection kept below the threshold of his own observation by self-medication.

The therapist, in late syphilis, must modify a symptomatic outlook with a preventive trend of mind. This will stimulate him to more complete examination, with a view to finding all the types of involvement in a given case.¹⁴ It will lead him to regulate the life of his patient so as to put the least possible strain on his weakest points, and to conduct his treatment so that an involvement just in its beginnings may not come to the front later as some more conspicuous symptom subsides.

The therapeutic test is so much more important in late syphilis than in early infections that attention should be called to some of its pitfalls. Therapeutic tests in general have meaning only when the patient presents a definite, and, as far as possible, a visible pathologic lesion, on which quantitative estimates of improvement can be made. Mere gain in weight, disappearance of indefinite pains, malaise or nondescript subjective symptoms are usually meaningless. Iodid therapeutic tests, popular with the departing generation, are untrustworthy. So are arsphenamin therapeutic tests. I have made, and seen made, erroneous diagnoses of gumma of the lymph nodes with partial positive Wassermann tests. I have seen tuberculous keratitis confused with syphilitic keratitis, lupus vulgaris, erythematous lupus, sarcoids, and tuberculids make striking improvement under arsphenamin. Mercury is probably more nearly immune from such nonspecific effects than either iodids or arsphenamin, although it is well to recall its action in lichen planus, and in occasional cases of sporotrichosis. Carcinoma of the stomach makes false responses to arsphenamin alone and sometimes in combination with mercury. One of the reasons a noted neurologist gave for object-

14. Studies of the multiform types of involvement often presented by patients with late syphilis seem to have been made largely by internists concerned with cardiovascular conditions. Compare also Footnote 13.

ing to the dermatologist as a syphilographer was his ignorance of the false positive therapeutic test for syphilis in multiple sclerosis. Pseudo-Herxheimer reactions in tuberculous processes occasionally create a deceptive effect.¹⁵

STANDARDIZATION OF TREATMENT

Standardization and routinization of the treatment of syphilis is much easier in the early months or years of the disease than in the late. Yet I would not for a moment substitute unlimited individualization for the good effects of system and regularity in the majority of cases. But back of any systematizing of treatment must lie a willingness to think of the disease as a whole, and of the patient as a human being. I have already sufficiently emphasized, in referring to the complete examination, the need of identifying every type of involvement in a given case. The same emphasis can be transferred to therapeutic management. In explaining to patients why I wish their eyes, teeth, tonsils, stomachs, bladders, and appendixes to have attention when their trouble is syphilis of the heart or of the liver, I often use the maxim of the service chief of the best automobile repair plant I know: "Don't listen to the owner's story about this creak and that rattle, and go by that. Go through the car and put her back as nearly as possible into the shape she was in when she left the factory." Do that with late syphilis and it will not need the experimental studies of a Brown or a Pearce to teach you that the course of syphilis is often as much modified by the things we leave undone as by the things we do. Bring the patient, in the course of your management of his case, as nearly up to the standard of normality for his age and sex as possible. Do, so far as possible, an overhauling and not a patching job.

In my few words concerning organized treatment I shall not even attempt an account of the endless variations proposed by different therapists. I do want to suggest, however, that we bear in mind a few principles. First, a heavy responsibility rests on the proposers of systems. Nothing is more eagerly sought after nor more frankly abused by the tyro, and even by the expert, than the rule of thumb. Yet, on the other hand, if there is any one factor which in my experience prevents the arrest or cure of syphilis, it is desultory and unsystematic management. In late syphilis, I believe, roughly speaking, in trying for radical results by combined spirillicidal and resistance-building methods,

15. The original observations on this point have been confirmed by my experience, Herxheimer, K., and Altmann, K.: *Weitere Mitteilungen zur Reaktion des Lupus vulgaris nebst Beiträgen zur Therapie desselben durch Salvarsan*, Arch. f. Dermat. u. Syph. **110**:249, 1911; *Ueber eine Reaktion tuberkulöser Prozesse nach Salvarsaninjektion*, Deutsch. med. Wchnschr. **1**:441, 1911.

rather than by the one or the other exclusively. Whether we obtain radical results or not, only time can decide. Life-long arrest means almost as much to the patient as extirpation. A frankly spirillicidal technic such as that of Pollitzer¹⁶ seems to me inapplicable to most of the cases which I am considering. I do not feel that its ability to reverse the Wassermann test, so frequently mentioned, is full and sufficient evidence of its effectiveness. It is too difficult to judge the extent and the type of involvement of important structures, even with the most careful preliminary examination, to justify a system of unqualified therapeutic bludgeoning. Recent continental opinion seems to be increasingly tending toward moderation, especially in the early months of the treatment of late syphilis.¹⁷ For the occasional patient with a high resistance to treatment and a threatening, though not as yet actually grave lesion, shortening of the intervals between arsphenamin injections, with large doses, is justifiable in endeavoring to reach an otherwise inaccessible focus. The favorable reports of users of such methods as Sicard's,¹⁸ with its enormous total and minute individual dosage, and the enthusiasm of the "Pollitzerizers," with their enormous individual and relatively small total dosages, are really tributes, not to any individual system, but to the wonderful variability of the disease and to that wide margin of safety for most patients, which enables almost any system that does not grossly violate the few outstanding rules of the game, to tip the delicate balance between progress and arrest, in the favorable direction. To my mind the essence of the modern treatment of syphilis is system and observation, and in the end those of the modern treatment technics which best perfect the *observational* aspect, will show the lowest ultimate mortality.

TREATMENT OF SPECIAL TYPES

May I, in a series of idiographic sentences, lay before you some of the high points of my observations on the treatment of special types of late syphilis?

16. Pollitzer, S.: The Principles of the Treatment of Syphilis, *J. Cutan. Dis.* **34**:633 (Sept.) 1916; Ormsby, O. S.: A Valuable Method of Employing Arsphenamin in Syphilis, *J. A. M. A.* **75**:1 (July 3) 1920.

17. This is especially true, of course, of vascular complications. Compare Kothny and Müller-Deham (Zur Neosalvarsantherapie beiluetischen Erkrankungen des Herzens und der Aorta, *Wien. klin. Wchnschr.* **33**:77 [Jan. 22] 1920), who review the German literature with reference to this question.

18. Sicard, J. A.: Traitement de la syphilis nerveuse, *Presse méd.* **28**:281 (May 8) 1920. The French seem to have had a penchant for small dosage, as witness Queyrat and Pinard (How to Cure the Syphilitic, *Médecine*, Paris **2**:101 [Nov.] 1920; abstr., *J. A. M. A.* **76**:143 [Jan. 8] 1921). Gougerot (Skin Diseases and Syphilis, *Medicine*, Paris **2**:85 [Nov.] 1920; abstr., *J. A. M. A.* **76**:143 [Jan. 8] 1921) states that the larger doses are gaining popularity in early syphilis.

Osseous Syphilis.—Arsphenamin deserves a conspicuous place for its promptness of action and the symptomatic relief which it affords in osseous syphilis.¹⁹ Since the Herxheimer reaction is unimportant, administration may be begun at once. Arsphenamin renders iodids unnecessary, as pointed out by Jeans. Cases with delayed response and much suppuration should be searched for sequestrums by roentgen-ray and direct examination; but surgical removal should not be attempted until after some months of intensive treatment.²⁰ Progressive osseous syphilis of the nose should be searched for epithelioma, and epithelioma in the nose may simulate late syphilis very closely, or be superposed on it. Mercury and arsphenamin administered together in osseous syphilis are more effective than either alone. Osteo-arthritis can be made to involute under treatment, but the Charcot joint when once fully developed, does not respond. No plastic work on bone syphilis should be attempted until after at least a year of intensive treatment, with a negative Wassermann reaction. The coincidence of negative Wassermann reactions with a still active syphilis of the nasal septum is responsible for more than one fallen bridge following operative interference. Hydrarthroses, not frankly of focal or tuberculous origin, should always have a therapeutic test. There is no object in making therapeutic tests on healed osseous lesions.

Cardiovascular Syphilis.—Cardiovascular involvement is probably present to some degree in nearly all late syphilis and should be searched for. The presence of obvious signs means a fairly advanced process.²¹ The condition of the coronary arteries, difficult to predict from either examination or history, is, I believe, very important. Necropsy experience has made us realize that patients who are seemingly good symptomatic risks may have such a degree of occlusion that death results under treatment from the Herxheimer reaction, or the effects of too rapid healing.²² Myocardial protest against arsphenamin, even in early cases, can be recognized by transient edema and a dilatation which

19. Jeans, P. C.: The Treatment of Hereditary Syphilis. Description of Method, with Discussion of Results After Four Years' Use, *J. A. M. A.* **76**:167 (Jan. 15) 1921.

20. For the surgical management of this complication in osteitis of the skull, when it is especially obstinate, compare Adson (The Surgical Treatment of Gummatous Osteitis of the Skull, *J. A. M. A.* **74**:385 [Feb. 7] 1920).

21. Reid's article is an excellent review of the findings in 105 cases, with a digest of the literature (Specific Aortitis, *Boston M. & S. J.* **183**:67 [July 15] 1920; cont. **183**:105 [July 22] 1920). Compare also Babcock (Some Practical Considerations with Regard to Syphilitic Aortitis, *Ann. J. Syph.* **4**:34 [Jan.] 1920) and Hoover (Aortitis Syphilitica, *J. A. M. A.* **74**:226 [Jan. 24] 1920).

22. I have been glad to find that my observations accord with those of Hubert from Romberg's clinic (Footnote 6).

responds to digitalis. Weeks or sometimes even months of mercurial preparation with inunctions and moderate doses of iodids are preferable to the immediate use of arsphenamin.²³ If arsphenamin is used the dosage should be small, and several observers have expressed a decided preference for neo-arsphenamin.²⁴ In dealing with combined neurosyphilis and cardiovascular syphilis, the cardiovascular lesion is usually the handicap and usually makes intraspinal treatment necessary. Aneurysms too early treated with arsphenamin, may rupture, and a certain amount of symptomatic advance, in the form of developing expansile pulsation²⁵ sometimes follows too rapid resolution of the mesaortitis and mediastinitis under intensive treatment. Rest in bed affects introspective and hyperactive types unfavorably, but cannot be avoided in threatened or actual decompensation. The anxiety neurosis of these patients is often more serious and obstinate than their syphilis. The patient must be reeducated to a matter-of-fact outlook and a uniform level of activity, without peaks of strain, reduced as the situation may require. At times even an assumed optimism in a consultant transforms the picture. Bromids are a valuable adjunct. Patients with cardiac disorders must be protected from gains in weight. Hypertension with an hypertrophied heart or a well compensated valvular lesion²⁶ has, as a rule, an excellent tolerance of treatment. Heroic iodid administration in cardiovascular syphilis has no special advantages over smaller dosage that we have been able to recognize.²⁷

Hepatic and Splenic Syphilis.—A liver palpable just below the costal margin following the first or second arsphenamin injection, with a slight tinging of the sclerae is sometimes all the evidence of diffuse hepatitis recognizable in a given case. Obvious damage to the liver calls for some caution with arsphenamin. On the other hand, the post hoc conclusion that all jaundice following treatment for syphilis is due

23. The various authors mentioned and their citations from the literature show that no unanimity of opinion on this point exists as yet. The value of arsphenamin, used with caution, is generally conceded now. Hirshfelder is a notable exception (*Diseases of the Heart and Aorta*, Ed. 3, Philadelphia, J. B. Lippincott Company, 1918, p. 346).

24. Kothny and Müller-Deham (Footnote 17).

25. Hubert (Footnote 6) gives orthodiagraphic evidence of the enlargement of the aneurysm. Goldscheider (*Über die syphilitische Erkrankung der Aorta*, *Med. Klin.* 8:471, 1912).

26. Hirschfelder (Footnote 23) and Reid (Footnote 21) discuss the fall in blood pressure due to arsphenamin as a contraindication.

27. Hoppe-Seyler: (*Die syphilitischen Erkrankungen der Bauch- und der Circulationsorgane [besonders der Leber und der Aorta] und ihr Einfluss auf die Felddienstfähigkeit.* *Med. Klin.* 10:1727, 1914) advocates iodid given intravenously.

to the medication is unwarranted.²⁸ The average patient with hepatitis, diffuse or gummatous, tolerates mercury well, and is the better for from two to six weeks of inunctions and iodids, or if much debilitated, mixed treatment by mouth with rest in bed. Only in the very late cases is exhibited the therapeutic paradox⁵ of increasing ascites with shrinkage of the liver. In my experience although transient ascites, or an increase of fluid with the Herxheimer reaction, is common, a true therapeutic paradox is rare. When it occurs, and tapping intervals grow progressively shorter, the Talma operation should be resorted to. The good results have been attested by Riesman.²⁹ The prognosis of hepatic syphilis, if treatment is not pushed too hard, and the patient is not moribund, is good, contrary to the usual belief.³⁰ Renal irritability is sometimes a serious matter, and demands much attention to foci of infection, diet, and so forth. Amyloid degeneration of the kidney, while a serious complication, does not flatly contraindicate fairly energetic therapy.

In marked splenomegaly the response of the fibrous spleen, in my experience, has not been very good, and when there is accompanying anemia, splenectomy performed by a competent operator yields good results.³¹ I have an impression that more effective therapeutic tests on splenomegaly would mean more syphilis recognized and fewer splenectomies performed.³²

Gastro-Intestinal Syphilis.—Gastric symptoms, excluding the frank crises of tabes dorsalis, are present in about one fourth of the cases of late syphilis.³³ If the clinical picture be other than carcinoma, with a positive Wassermann reaction, therapy takes precedence over operation. This is, of course, especially true of hour-glass deformities. But if carcinoma is the probable diagnosis and operability prospects are good, exploration should come first and treatment second, if the findings at exploration confirm the diagnosis of syphilis. Persistence of gastric

28. Syphilitic acute yellow atrophy (toxic hepatitis) is not considered here, since it is an accompaniment of early syphilis. A key to the recent French quasi-polemic writings on this subject can be obtained from Milian (Footnote 8).

29. Riesman, D.: Spontaneous and Operative Cure of Cirrhosis of the Liver. Report of Illustrative Cases. *J. A. M. A.* **76**:288 (Jan. 29) 1921.

30. Wile (Footnote 5) takes the opposite view; McNeil (*Syphilis of the Liver*, *Am. J. Syph.* **1**:738 [Oct.] 1917) agrees with me.

31. A recent complete summary of the status of splenectomy in therapeutics is that of Giffin (*Present Status of Splenectomy as a Therapeutic Measure*, *Minnesota Med.* **4**:132 [March] 1921).

32. Eason, J.: The Treatment of Splenomegaly with Anaemia in Syphilites. *Edinburgh M. J.* **21**:258 (Nov.) 1918.

33. This is the experience of the Mayo Clinic as summarized by Stokes and Brehmer (*Syphilis in Railroad Employees*, *J. Indust. Hyg.* **1**:419 [Jan.] 1920).

symptoms in other than frank crises, after the first few weeks of treatment, calls for further search, in which an astute clinician will often be rewarded with the finding of duodenal ulcer, appendicitis, or other pathologic conditions, slighted or lost sight of when the positive Wassermann reaction was found. Persistent morning nausea, instead of periodic attacks, has in my experience sometimes been a symptom of morphinism complicating gastric crises. In this connection, I cannot refrain from protest at the readiness with which physicians at large prescribe morphin for spasmodic abdominal pain. The tradition has cost lives; for there are few problems more unmanageable than a morphin addict with crises. Arsphenamin is the drug of election in gastric syphilis. The response is one of the most gratifying in the entire field of late syphilis, and seems but rarely dependent on the extent of anatomic change as indicated by the roentgen ray, except in the case of linitis plastica.³⁴ A gain of 100 pounds in weight occurred in a patient in whom, at necropsy following influenza, a stricture 10 cm. long near the pyloric end of the stomach, was found which would not pass a lead pencil. The starvation acidosis in these cases may need consideration. With involvement of the esophagus and of the rectum, the outlook is proportional to the ratio between active inflammatory infiltration and scar. Patients in the late stages have a poor outlook for medical relief.

Renal Syphilis.—Before instituting therapeutic tests for gumma of the kidney one should be reasonably sure that one is not dealing with hypernephroma. Infected kidneys react unfavorably to arsphenamin. Other types of nephritis and nephroses tolerate it much better than mercury, and it may be employed with a phenolsulphonephthalein output of zero without ill effect, provided this low function be not due to urinary retention. Therapeutic tests for syphilitic nephritis are not always infallible, even though the nephritis may respond, at the outset, to some extent to arsphenamin. A nephrosis with a high albuminuria, in the absence of blood and casts and with normal function, may develop late in a vigorous course of treatment.³⁵

Anemia in Syphilis.—The severe anemias which form a rare complication or accompaniment of late syphilis respond, on the whole, better to arsphenamin than to mercury, although neither is able permanently to influence the course of a pernicious type in the very large

34. Sailer (Linitis Plastica, *Am. J. M. Sc.* **157**:321 [March] 1916) advises treatment for syphilis when linitis plastica is associated with a positive Wassermann reaction. The occurrence of structural improvement in gastric syphilis has been demonstrated by Eusterman (*Syphilis of the Stomach: A Clinical and Roentgenological Study with a Report of Twenty-Three Cases*, *Am. J. M. Sc.* **153**:21 [Jan.] 1917).

35. Lankhout (*Syphilis and Kidney Disease*, *Nederlandsch. Tijdschr. v. Geneesk* **2**:2649, 1920; abstr. *J. A. M. A.* **76**:626 [Feb. 26] 1921).

majority of cases.³⁶ In fact, I have seen only one case of primary anemia in which the response led me to expect a cure. Avoidance of reactions is highly important. The occurrence of false positive Wassermann reactions in primary anemias has led to more than one disappointing therapeutic test. Anemias of secondary type, of great persistence, largely uninfluenced or at most only temporarily influenced by any form of treatment, occur in late syphilis. One that I recall responded to removal of a septic gallbladder.

Wassermann-resistant patients,³⁷ instead of being dismissed with reassurances, need, I believe, intensive study and lifelong observation. Paradoxically, however, I do not believe the reversal of the Wassermann reaction to be an end in itself, since its relation to the structural or functional integrity of any organ is as yet obscure. As one's experience with modern therapy increases, fixed positive reactions become fewer, especially following the prolonged use of inunctions. The Pollitzer technic is especially extolled³⁸ as a means of reversing resistant cases, but should only be used after a comprehensive survey of the case. Other conditions besides paresis may underlie an irreversible test. The reputed resistant Wassermann reaction in children has not materialized in either Jeans'³⁹ experience or my own. I have seen nothing to confirm Strickler's³⁹ impressions as to the influence of arsphenamin in the production of false or persistent positives.⁴⁰

Syphilis of the Eye.—I am returning to Ehrlich's original belief that arsphenamin is distinctly contraindicated in some cases of simple primary optic atrophy (not secondary to neuroretinitis or choked disk), at least in the early months of the course. I have seen a patient with good vision go totally blind with four arsphenamin injections, and another, with primary optic atrophy, due to high myopia, have to be transferred to mercury because of its action. On the other hand, focal infections in the mouth, stirred up by mercury, occasionally cause trouble from the other direction. Treatment for syphilis, especially with arsphenamin and the iodids, has marked nonspecific effects in the eye.

36. Gorke (Auftreten von apastischer Anämie nach Salvarsan, München, med. Wchnschr. **67**:1226, 1920). Compare also Footnote 9.

37. Footnote 13. Compare also Wile, W. J., and Hasley, C. K.: Serologic Cure (?) in the Light of Increasingly Sensitive Wassermann Tests, J. A. M. A. **72**:1526 (May 24) 1919.

38. Footnote 16, first reference.

39. Strickler, A., Munson, H. G., and Sidlick, D. M.: A Positive Wassermann Test in Non-syphilitic Patients After Intravenous Therapy, J. A. M. A. **75**:1488 (Nov. 27) 1920.

40. For a critical consideration of the merits of this question, compare Kolmer, J. A.: The Question of Positive Wassermann Reactions Caused by the Intravenous Administration of Arsphenamin, correspondence, J. A. M. A. **75**:1796 (Dec. 25) 1920.

which could be more widely utilized in the treatment of uveitis, episcleritis, tuberculous keratitis, and so forth. Ophthalmologists are all too unfamiliar with the effect of arsphenamin on interstitial keratitis, which is an immense advance over the effect of mercury, although it must be combined with it for permanence. The value of months and years of persistence in seemingly hopelessly impaired cases has been impressed on me.

Syphilis of the Ear.—Deafness in hereditary or acquired syphilis should always be intensively treated, regardless of its duration. The occasional patient exhibits unexpected improvement (test it by speaking from behind the patient to keep him from reading lips). In acute onsets I prefer mercurial preparation, but I have seen no ill effects from arsphenamin. Patients with associated neurosyphilis may make an especially good response. Patients with positive B \acute{a} r \acute{a} ny reactions may make some objective improvement, but I believe the specificity of this response is still open to question.

Syphilis of the Nose and Throat.—The response to arsphenamin is miraculous and sometimes life-saving, when deglutition has been obstructed, but if the process involves the larynx or trachea, the immediate use of this drug, even in seemingly trivial lesions, is dangerous because of the Herxheimer reaction. Provocative procedures must not be used in such cases. On the tongue, the coincidence of lesions undergoing malignant changes and new crops of recurrences is possible. I have seen hemiglossectomy performed for carcinoma on gumma, while later, because no treatment was given for the syphilis, another gumma was allowed to develop and degenerate on the other side. The confusion of the pathology of gumma with that of tuberculosis of the tongue (so-called "tuberculoma") with a positive Wassermann reaction is more common perhaps than is realized.

SYPHILIS IN MOTHER AND CHILD

Syphilis in the mother⁴¹ is one of the richest fields for prophylactic effort now available, as indicated by the steady influx of favorable reports of the work of obstetric services and prenatal care clinics,⁴²

41. Skinner (Syphilis at a Venereal Clinic: An Analysis of Cases Admitted During Twelve Months, *Lancet* **1**:650 [March 20] 1920) points out, however, how few women report for examination or treatment short of a fully developed infection.

42. Williams (The Significance of Syphilis in Prenatal Care and in the Causation of Foetal Death, *Bull. Johns Hopkins Hosp.* **31**:141 [March] 1920) found 53 per cent. syphilitic children of untreated mothers, 7.4 per cent. of mothers treated during pregnancy. Compare also Adams, J.: Treatment of Ante-Natal and Post-Natal Syphilis, *Brit. M. J.* **2**:541 (Nov. 16) 1918; and Chambrelent: La mortinatalit  en France. Elle est evitable dans la majorit  des cas, *Nourrison* **8**:321, 1920.

in which the problem is beginning to receive the attention it deserves. Syphilis in the child should receive the same treatment as syphilis in the adult, in response to a growing appreciation that apart from stigmatization and the high mortality of untreated uterine infections, it presents no essential differences. In fact, the surviving untreated child has a resistance that is a valuable asset in treatment. Instead of boring you with a recital of technical details, let me summarize what I conceive to be essential principles. The relative immunity of the woman from external manifestations of the disease and the suppressing effect of pregnancy and lactation has placed syphilis in women in a field by itself. The institution of therapy for the protection of the child seems to me justified in women in whom evidence of syphilitic infection is so doubtful that the advisability of treatment would be questionable under other circumstances. The studies of Widakowich⁴³ on spermatozoal anomalies and the findings of Eberson³ in the male syphilitic furnish the first tangible hint of direct paternal influence⁴⁴ and raise the question of whether or not the father should have treatment as a preparation for conception quite as much as the mother for gestation. This constitutes what I have both preached and practiced as "treatment for life insurance" in the parents of a syphilitic child. Of late I have grown almost radical enough to believe that at no time can the woman who has had syphilis be advised to go through pregnancy without a treatment course coincidently. While this would bear hard on the mother of nineteen children, it need not be a hardship to the average family, and might, if observation of the children thus born should justify it, permit a relaxation of rules with respect to marriage.

Spirillicidal methods must be a prominent feature of the treatment of the pregnant woman, since a maximum destruction of organisms is, at least so far as our present knowledge goes, the best protection to the child. There seem to me to be good reasons for giving from one half to two thirds of the full doses all around, to the pregnant woman. Her infection is to some extent inhibited by her pregnancy;⁴⁵ her liver and kidneys are both under strain, as evidenced by the familiar intoxi-

43. Widakowich, V.: The Spermatozoa of Syphilitics, *Semana med.* **27**:633 (Nov. 11) 1920; abstr. *J. A. M. A.* **76**:414 (Feb. 5) 1921.

44. Routh (Antenatal Syphilis: Suggested Action of the Chorionic Ferments, abstr. *Brit. M. J.* **1**:47 [Jan. 12] 1918) makes an interesting argument for a paternal factor on the basis of Noguchi's spirillolysis, attempting also to explain delayed infection of the fetus in untreated cases.

45. Brown, W. H., and Pearce, Louise: On the Reaction of Pregnant and Lactating Females to Inoculation with *Treponema Pallidum*—A Preliminary Note. *Am. J. Syph.* **4**:593 (Oct.) 1920.

cations of pregnancy, and her metabolic and eliminative mechanism therefore cannot be equal to massive treatment.⁴⁶

Whether the child born symptomless will remain so, is the crux of the prophylactic phase of treatment in mother and child.⁴⁷ The possibility of long periods of latency after birth in children treated during uterine life, familiar in the untreated infection as well, demands the fullest development of facilities for the following up and observation of the syphilitic family before the cure of the child by treatment of the mother is accepted as established.

Systems of treating the child show a commendable trend toward increasing intensity, tempered by the realization that most uterine syphilis is late syphilis.⁴⁸ Fordyce and Rosen's⁴⁹ advocacy of intramuscular arsphenamin is intended apparently to popularize the drug with those technically inexperienced.⁵⁰ I agree with Jeans¹⁹ that the expert seldom or never has need to use other than the intravenous route.⁵¹ The tolerance of children for mercury is proportionately greater, I believe, than that of adults, and the intramuscular and inunction routes are gaining a well-deserved popularity. As a relief from the debilitating effects of prolonged mercurialization, arsphenamin is even more welcome in the treatment of children than in that of adults. The synergistic effect of the two drugs is also valuable in obstinate cases. Intraspinial measures have been effectively used.

The conception of the Weylander school-hospital for the combined treatment and education of children with heredosyphilis has not received the attention it should have in this country. The reports from the Scandinavian countries and Germany indicate that it solves the problems of hospital care and social rehabilitation.

46. Adams (Footnote 42, second reference) praises liberal doses of arsphenamin for mothers, but his mercurialization is practically all by mouth. Williams (Footnote 42, first reference) does not specify his technic, but it seems to have been conservative.

47. Much rather unguarded emphasis is being placed on the child's negative Wassermann test after birth.

48. Veeder, B. S., and Jeans, P. C.: The Diagnosis and Treatment of "Late" Hereditary Syphilis. *Am. J. Dis. Child.* **8**:283 (Oct.) 1914.

49. Fordyce, J. A., and Rosen, I.: A Method of Treating Congenital Syphilis. *J. A. M. A.* **75**:1385 (Nov. 20) 1920.

50. Adams (Footnote 42, second reference) commends galyi in glucose, one seventeenth of the adult dose.

51. It would be interesting to apply the proportionally huge doses of neoarsphenamin by rectum, employed by Mehrrens (Rectal Injections of Massive Doses of Neo-Arsphenamin, *J. A. M. A.* **76**:574 [Feb. 26] 1921).

CONCLUSIONS

This rather cursory review of the principles underlying certain special phases of syphilis will defeat its own purpose if it leaves the impression that the treatment of the disease should be parceled out in segments, each self-sufficient and governed by its own laws. Just as we are finding that early syphilis is no longer localized, even at the earliest appearance of the primary lesion, so we shall find as the intensity of our study increases that late syphilis does not begin in the first decade, but in the first hour. Preventing the transmission of the disease in its earlier stages, and forestalling the individual tendency to complications based on the peculiarities of the strain of parasite, the host, and the method of treatment, is the whole problem of syphilis. Forestalling implies detection, so that an increasing diagnostic alertness, a development of methods for detecting the earliest and not the late signs of pathologic change in vital organs and tissues, is not mere diagnosis, but a part of effective treatment. For all our so-called prophylactic effort, nothing will prevent the development of late complications in a certain group of patients who present the fatal combination of predisposed soil and tropic organism. It is equally true that an even smaller group of patients will master the infection for themselves, irrespective of our interference. Between these two extremes will come those whom we have radically cured, those whom we have managed to place in commensal relation to their infecting organism, those whose immunity we have broken by treatment measures whose potentialities for future harm as well as present good we do not yet understand, and those whom we have destroyed outright by treatment itself. The study of the interrelation of these groups is one of the most complex problems of the medicine of today. Its solution will not be accomplished by a mental or a physical separation of the various phases of syphilis and syphilotherapy into air-tight compartments each with its own technic, ideals and aims. Only that mode of approach will leave a significant impress on our future knowledge which envisages the entire disease, employs one or two methods in a large series of cases over a period of many years, records the results, and which, by lifelong observation and periodic complete reexamination, detects impending serious pathologic change, and evaluates in detail and with accuracy the response of parasite and host.

CRUDE COAL TAR IN DERMATOLOGY*

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Some years ago, Brocq published a note on the use of crude coal tar in cutaneous diseases. He recommended the application of the substance to weeping surfaces in 100 per cent. strength, and he wrote enthusiastically of its beneficial effects.

This note reached America, and at the Massachusetts General Hospital we seized on the idea at once and from that day to this have been ardent devotees and advocates of the drug. Crude coal tar, as you all know, is one of the two or three primary by-products in the manufacture of coal gas and, in the early days, our hospital apothecary used to send a boy and a pail to the gas house to procure this dirty, ill-smelling, black, but withal wonderful, substance. Later on, as we began to employ the drug more and more, we found that it had been commercialized by the Eastern Drug Company of Boston and from this house all Boston apothecaries now derive their source of supply. Personally, I feel that we do not get quite so brilliant clinical results from this modern method; but this is only a feeling, I admit.

At first we confined ourselves to Brocq's teachings and used 100 per cent. crude coal tar on moist surfaces. We had some brilliant successes and some failures, but proportionately many patients complained of smarting and burning. We therefore reduced the strength of the drug to 5 per cent., incorporating it in our zinc paste and, except in rare instances, have used the tar in this proportion ever since. Our formula reads as follows: \mathcal{R} crude coal tar 2, zinc oxid 2, cornstarch 16, petrolatum 16. In prescribing this drug, we must be very sure of the reliability and of the special knowledge of the apothecary who is to compound the prescription. We must always be on our guard to see that he does not use any vegetable tar in place of this definite mineral product, and we must be equally sure that he knows in what sequence to combine the various ingredients of our prescription. The one and only proper method is as follows: first, mix thoroughly the cornstarch and the petrolatum; second, rub together the coal tar and the zinc oxid; third, combine the first product with the second. This method produces a nearly black, perfectly smooth paste, which smells strongly of coal gas and tar. These two injunctions are absolutely essential to success. A vegetable tar of any sort is always too strong

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

for use in dermatoses which call for the mineral product, and a faulty combination of the ingredients produces an olive-green compound which does not smell of coal gas and which proves very irritating and frequently even pyogenic.

The proper methods of application and removal of this paste are also to be carefully detailed to the patient. Always cut all involved hair short when possible. Never bandage crude coal tar—pustulation is the result if this injunction is disobeyed. Smear on a medium coating of the paste with a wooden throat stick, and cover over the part with one thickness of old cotton or linen. Thin white cotton gloves may be advantageously substituted when we are treating the feet and ankles; and the footless legs of white cotton stockings may be drawn over the arms or legs of the patient. All of these dressings must be washed and boiled every twenty-four hours. The same crude coal tar should never be allowed to remain on the human skin for more than twelve hours; we must always guard against the peculiar follicular pustulation which this drug can produce, if improperly used. We must, therefore, be sure to remove every vestige of the previous application before making the next dressing, and this may be easily accomplished by means of sterilized gauze, soaked in the oil of sweet almonds or in olive oil.

One further point must be thoroughly explained to the patient. Crude coal tar necessarily discolors bed and body clothing. To wash such clothes in the ordinary way with soap and water means an indelible battleship-gray stain throughout the future life of the linen. This unfortunate result can be obviated very easily by impregnating the discoloration from both sides with lard, and after an hour or more the linen can be washed with a pure white soap and warm water, and all signs of the spots will have vanished.

Brocq originally limited his advocacy of crude coal tar, if I am not mistaken, to the treatment of moist varicose ulcers. We copied him and were delighted with our results. From that time on we have gradually extended the use of the drug until now we feel reasonably justified in recommending it in the following diseases or conditions: infantile eczema; moist eczema of adult life; moist examples of eczema seborrheicum of the scalp, especially the frontal type; pruritus ani et vulvae; neurodermite, especially of the occipital type in middle-aged women; the chronic papular urticarias which border on prurigo, and the very moist types of epidermophytosis.

INFANTILE ECZEMA

Infantile eczema was the first disease in which we left the narrow path indicated by Brocq, and we have never regretted our deviation. Today, after several years of increasing experience, we feel justified in saying that crude coal tar has revolutionized the evolution of the

disease. Formerly, infantile eczema meant, to me at least, the loss of nearly the first two years of the unfortunate child's comfort and happiness, with the intervening summer more or less included; it meant the careful preparation of innumerable face masks, the constant tying of the baby's hands and the need of two pairs of attendant hands when the child was to be bathed or its clothes changed; it meant the despair of the child's parents and the attendants; and it meant the chagrin and discouragement of the visiting dermatologist. Now this unfortunate experience is practically a thing of the past, for with our present knowledge of the use of crude coal tar, of the value of the fecal examinations and of cutaneous tests, it is a rare occurrence to find the disease lasting more than a few months at most.

The procedure may be thus described. The black paste is to be smeared on the child's face or buttocks, or wherever necessary. This is done twice a day, after careful removal of all remnants of the previous application. No bandages are to be applied but, if necessary, at first, the patient's sleeves are to be fastened with strong safety pins to the diapers. The child is not to be taken into the street, but may be placed on a carefully screened piazza or balcony, if such is available. If this is impossible, the child is to be left in a room with the windows open, the heat turned on and the crib scrupulously guarded from the wind and the sun. When the time comes for feeding, or for the prompt changing of the diapers (a very necessary precaution in case of involvement of the buttocks or genitalia), the baby is taken to a warm room but returned as soon as possible.

At the end of a week, if all injunctions have been conscientiously obeyed, we may expect a marked improvement. We then continue as before, until the eruption entirely disappears or until improvement ceases. In the latter case, we ask for a macroscopic and a microscopic examination of the feces by an expert, and we count on finding, in the majority of these disappointing reactions to the drug, positive results which may be roughly summarized thus: If the eczema is of the wet type, we may expect evidences of fat indigestion; if the disease is of the dry variety, starch is usually the factor at fault. In my experience, proteins are rarely the mischief makers. We then try to rectify the diet and continue with the crude coal tar. In another two or three weeks, if failure pursues us, we try the cutaneous tests; but such a contingency is rare.

In passing, let me say that the moist types of eczema are much more amenable to the good influences of crude coal tar. Let me also add one further word of caution. Do not attempt, while pursuing this treatment, to use any other drug in ointment form. Crude coal tar is a jealous handmaid, and causes trouble if any outside aid is employed. Often

have we made the mistake, when the worst phases of the disease have passed, of thinking that we could finish the treatment by using some less dirty drug. We never attempt this method now. If you begin with crude coal tar in infantile eczema, carry through to the end with this drug and with no other. If you fail, however, after calling on all the other resources detailed, try something else. Often, after the first week or two of treatment with the 5 per cent. strength of the drug, we find the skin becoming rather wrinkled. This means that the drug is proving too drying—then reduce its strength to 3 per cent., and continue. This is a legitimate proceeding and no harm is done.

This is my conception of the use of crude coal tar in the infantile eczema. Some of these many details may seem trivial, but long experience with the drug has taught me much.

THE MOIST ECZEMAS OF ADULT LIFE

There are certain types of adult moist eczema which seem to be peculiarly amenable to the influence of crude coal tar.

The first variety is that found just above and just behind the ears. In such instances we suspect the irritating contact of spectacles, or, again, of dyed or very seborrheic hair; but we must confess that at times none of these trouble makers is present. This variety of eczema has proved in the past very obstinate to deal with, but under the influence of crude coal tar we are now accustomed to see it dry up and fade away day by day, until within a comparatively short time it has gone for good. Here again we must see the cure to its end, with crude coal tar alone.

The second example of moist eczema is not so limited in location as the aural one just described. It usually is found in good sized patches, most frequently on the lower part of the lower legs, next on the lower arms and, finally, in scattered smaller areas on the trunk. In former days we were wont to seek relief from black wash, but now we call on crude coal tar and are seldom disappointed. In some instances of this type, especially on the lower legs, the moisture is so excessive that we feel at liberty to use the drug in 100 per cent. strength at first, in a few days dropping down to our usual 5 per cent. paste. When the drug is used in this form we apply it on an absorbent cotton swab, and then anchor it by dusting some absorbent powder over the area. One application will last for several days, but a great objection to this otherwise efficacious method is the difficulty of removing the tar without irritating the underlying delicate skin.

MOIST ECZEMA SEBORRHEICUM

There are certain types of cephalic eczema seborrheicum which are peculiarly moist, and, *ipso facto*, perhaps, are peculiarly recalcitrant to

treatment. Sometimes this variety is limited to the forehead and frontal scalp and sometimes to its frontal, parietal and mastoid peripheries. The affected skin is strangely yellow-red, and covered with oily sebum to such an extent that impetigo contagiosa is strongly simulated. I have seen this form of the disease resist all of our time-honored suitable drugs and then yield within a week to the sedative, desiccating effects of crude coal tar. Eczema seborrheicum of the body on the other hand is not often influenced by the drug.

When crude coal tar is to be applied within the hair, we must alter our procedure somewhat. The drug is combined, in this instance, with zinc oxid and petrolatum only, in order to thin down the preparation. Applications are made directly to the scalp along successive partings, at intervals of one quarter inch, by means of a minimum amount of absorbent cotton wrapped around the end of a wooden toothpick. The drug is removed the following morning by means of olive oil. Soap and water are thus avoided, and should be strictly tabooed.

PRURITUS ANI ET VULVAE

As you know, volumes have been written on the treatment of pruritus ani. Dermatologists have recommended this drug and that; surgeons have advocated divulsions and dissections; and more recently bacteriologists have spoken highly of vaccines. All of these methods are expensive and admittedly time-consuming, and entail many failures. The old adage that many methods of treatment signify a lack of any good one holds strikingly true in this disease. Nevertheless, I believe that few individuals who are willing to try crude coal tar in the proper manner, carrying out all details to the letter, will ever need to look elsewhere for a cure, and a rapid one at that.

Before beginning this treatment, we ask the patient not to lead too sedentary a life, not to take too stimulating food or drink, not to live at full speed and not to be constipated. We ask him to cut the peri-anal hair and after defecation to clean the anus with moist, thin tissue paper and to dry the part by firm pressure with absorbent cotton. We advise him in bathing not to use soap about the anus, and to dry this region with absorbent cotton and firm pressure and not by see-sawing back and forth with a towel. After defecation and once again at the end of the day, we ask the patient to squat down on his haunches with a mirror placed on the floor in such a way that he can clearly see the whole anal region, and we instruct him to take a wooden toothpick with an absorbent cotton end smeared with crude coal tar paste and to paint the paste most carefully into the depth of every peri-anal sulcus. Swabbing the brush back and forth will accomplish nothing. In our instruction we liken the process to the painting of a wheel with the anal opening as the axle hole and the ribs between

the radiating sulci as the spokes—only in this instance we paint the areas between the spokes and not the spokes themselves. In my opinion the trouble, probably bacterial or mycologic, lies in the depths of these folds and I believe that the settlement of the whole problem depends on reaching these depths with the proper medicament. These complicated instructions are not idle words, trivial as they may sound. I always tell my students that one great secret of success in dermatologic therapeutics lies in the art of taking pains.

The treatment of vulvar itch is much simpler. We must be sure that there is no complicating sugar in the blood or any question of pediculosis or epidermophytosis. We then advise the cutting of the local hair and the application of the crude coal tar twice a day.

NEURODERMITE

Under this title I want to refer especially to the suboccipital infiltration, dry scaling and underlying redness found principally in women, and during the menopause, but I wish also to consider the lichen circumscriptus of other parts of the body and finally the general lichenification which may betoken leukemia or may draw near to papular urticaria and prurigo.

Neurodermite of the scalp was always a stumbling block therapeutically until the advent of crude coal tar. It is now most docile to treatment. Time is required, to be sure, but one does not necessarily expect to be cured of a most chronic condition in a moment. The drug should always be applied by a conscientious friend or relative. Every night numerous vertical partings of the hair are made and so directly on to the skin the crude coal tar, zinc oxid and petrolatum are smeared in the smallest quantities possible by means of the fine swab of absorbent cotton twisted around the end of a small wooden toothpick. By this means the messing of the hair is practically avoided, and in the morning what is left of the ointment can be most satisfactorily removed in exactly the same way, by means of olive oil. Nothing is applied during the day. Remember that crude coal tar will not tolerate the contemporaneous use of any other ointment. By this method, the month- or year-long itching and the hitherto uncontrollable desire to scratch are often so alleviated that real help can be obtained almost at once, and with the cessation of scratching slow, or rapid and progressive, progress toward cure is effected.

With lichen circumscriptus of the leg or of other parts of the body or extremities, crude coal tar is in no way comparably successful, but with the exception of the roentgen ray or radium there does not seem to be anything more effective than crude coal tar.

With large areas of the fiercely pruriginous, leathery, tough, pigmented, minutely scaly skin, composed fundamentally of lichenified papules, which accompany certain instances of leukemia and most obstinate papular urticaria and prurigo, crude coal tar may prove most highly and surprisingly efficacious, but again may fail dismally when it comes to permanent relief. As witness to the successful issue, let me cite the following cases, not unique by any means. In these instances the drug was used in 100 per cent. strength.

REPORT OF CASES

CASE 1.—J. L. G., aged 26, a clerk, reported March 28, with a condition of nine years' duration. He had been to all the hospitals and had tried everything, including crude tar. He could not stand ointment. Washes soothed, but did not cure. There was a universal involvement of the skin which was leathery to the feel and snowy to the sight, presenting many deep excoriations. Crude coal tar 100 per cent. was painted on at night. A wash of phenol 2, calamin 4, zinc oxid 8, glycerin 8, distilled water q. s. ad 250, was applied by day when itching required; and starch baths (one pound of cornstarch to the tub; temperature of water from 90 to 95 F.) with Gibbs' superfatted cold cream soap were taken at night.

By April 5, an extraordinary change was noted. "Friends inquired in the street what has happened." To the eye there was little visible, save a red nose and some redness and infiltration of the central part of the face.

By April 21, practically nothing was left; only a half dozen lesions, and these were merely frontal, self inflicted excoriations. "People can't believe their eyes." Shaving was no longer irritating. The sun, however, was troublesome.

CASE 2.—F. S. H., aged 46, a dentist, presented himself for treatment with a 3-inch square lichenified patch on the lower part of the leg, of one year's duration and many pea-sized, infiltrated, excoriated, lichenified papules on the arms, of more recent origin. Crude coal tar 100 per cent. was prescribed.

March 14, the arms were practically well; all itching was gone. The area on the leg had greatly improved. The patient did not return.

CASE 3.—Miss D. G. D., aged 27, following three injections of some vaccine or serum as a preventive against cerebrospinal meningitis in August had an attack of urticaria and now, despite considerable treatment by the family physician, there were a few wheals and a great number of dull red or brown, deeply infiltrated and excoriated papules. December 3, crude coal tar was prescribed. January 3, the patient writes that she "is cured."

EPIDERMOPHYTOSIS

In this disease there are two phases in which crude coal tar may prove of distinctive benefit. The more common one is the moist, eczematoid condition in which, through overstimulation, friction or other irritation, the skin becomes raw and red and distinctly uncomfortable. The much rarer type is found usually on the upper inner thighs, where through long-continued scratching a chronic patch becomes lichenified. In these two varieties of this common infection, crude

coal tar is not curative, but as a palliative and sedative desiccant it is highly successful. When the drug has done its expected service, we continue the destruction of the infecting agent by more appropriate means.

This brings me to the end of my theme. It is evident that I am a believer in the efficacy of crude coal tar, granted that it is used in the proper place and in the proper manner. I believe that Brocq's introduction of this drug has constituted one of the greatest dermatologic therapeutic contributions in modern times.

ABSTRACT OF DISCUSSION

DR. HARVEY P. TOWLE, Boston: In estimating the efficiency of crude coal tar in the various dermatoses there is one thing that must be considered: There are various kinds of crude coal tar on the market. Some of them instead of being soothing are irritating. Crude tar itself is a very irritating substance and it should, before being used, be thoroughly washed. One druggist in Boston does not trust the ordinary supply houses but washes the crude tar himself, and certainly the preparations we get from his store are much better than those obtained elsewhere.

DR. HARRY G. IRVINE, Minneapolis: I wish to apologize to the Association first for placing a paper on the program and then asking to withdraw it. At the time I presented the title I did not know, of course, about Dr. White's paper, and when I saw he was on the program for a paper on the same subject it seemed to me there was not enough ground for both papers. There would be sure to be a great deal of repetition and I thought additional points could better be brought out in the discussion.

I think we owe a great deal to Dr. White for his work with the crude tar. So far as I know there is not a textbook that mentions crude tar at all, at least not to any extent. The principles of the tar treatment as we have taught them in the past have been revolutionized. We have taught students not to use it when inflammation or acute eruptions were present; but quite the contrary is true of crude coal tar, because it can successfully be used under these conditions.

The coal tar industry probably originated with a German chemist in the latter part of the seventeenth century when he described a method of making peat and pit coal into coke and also the tar from these which was used to preserve ropes and wood. For a long time tar was simply a nuisance incidental to making coke and later in making gas. The first public gas works was in London, in 1813, then in Paris, in 1815, and in Berlin, in 1826. From about 1830 to 1838 tar began to be used as a preservative and for some by-products. Later, in 1856, they began to develop the anilin dyes and since then it has been of vastly greater importance. The two principal sources of tar are the gas works and the coke ovens. The formula varies with the manufacturer. Many of the by-products have become extremely valuable, and the manufacturers vary their process according to which by-product they wish to produce. This varies the crude tar. It is necessary to know where the tar comes from in order to produce the results brought out by Dr. White. You cannot go to the gas house for tar in any city and get the same results, because the tar varies. It varies in the way the heat is applied. If it is applied slowly, one product is obtained; if it is applied quickly and run up to a high degree, a very

different product is the result. The shape of the retort also varies the tar as well as the kind of coal. Crude tar is an extremely complex substance, and we must bear all these things in mind before we put down that we can do so and so with crude tar, because we cannot get the same results with all tars. Much more work must be done with the chemistry and with the constituents before we can lay down any arbitrary rules to govern its therapy. With low distillation we have more phenols and toluene, and in high distillation, used ordinarily in the gas house, we have more benzene, more naphthalene and anthracene, and far more free carbon, a very different product. Vertical retorts produce a tar with almost 50 per cent. less naphthalene than horizontal retorts. In more recent years, when distilling the coal for the tar itself, or for the coke, the tar has been more uniform and different from the gas house tar, but the question remains to be settled as to which is the best therapeutic product.

All these things must be brought out carefully before we lay down hard and fast rules. I think Dr. White is to be congratulated particularly for his very keen observation on what might appear minor details, his careful deductions and the principles he has laid down for using the preparation. They cannot be followed too closely to get success. There are properties in the tar which are extremely irritating. The pitch was investigated as early as 1909, by Ehrman, on account of what was called "pitch cancers." So many workers had this form of dermatitis that in England many factories had strict rules concerning it and provided places where employes could wash, and so attempt to avoid this dermatitis. Whether this is due to a certain type of tar or to something else, we know that frequently we find in workers a type of dermatitis with large bullae. One may be greatly astonished to have a patient come back with these large bullae, as large as the end of a thumb, with no pustules, and without any explanation.

As to the types of cases, we have had about the same types as Dr. White, with about the same results. We have changed his formula a little; instead of so much starch we use a little hydrous wool fat and think it is a little nicer product although it is no more efficient. We also have another type in which we mix acetone, collodion and tar in equal parts which is very convenient. It does not need to be bandaged and does not come off on the clothing, but it seems to be inefficient in certain types of cases. A single application of the crude tar in twenty-four hours produces wonderful results in many instances. I have not seen any of the cases of lichen simplex chronicus go on to complete cure and think we still have to handle them with the roentgen ray.

In psoriasis, I think we should sound a warning in cases in which large areas are involved, as there seems to be absorption of some constituent, perhaps the phenol, which is present in 2 or 3 per cent., and which has a toxic effect. We have had some patients complain of a severe "kick" the day following the application when it was used on large areas. In cases with small areas involved, it has worked very well.

This paint can be used in impetigo quite as efficiently as silver nitrate and is more easily removed.

We have recently been trying it on a typical case of parapsoriasis, simply as a matter of experiment. There seems to be a distinct fading of the lesions, which have been present for nearly a year, after the application of this paint. It seems to have had some effect in this disease in which there is so little to be done.

DR. HOWARD FOX, New York: I agree with Dr. Irvine that Dr. White should be congratulated for bringing to our notice an extremely valuable drug and one that has not received the recognition it deserves. I have had a real coal tar orgy during the past year with cases in the hospital and my private practice, and have been astonished at the results obtained. I have used the pure, crude coal tar (obtained from the gas house) in pure strength, using it in various forms of eczema, particularly the oozing type in infants and adults and in various forms of Duhring's disease. I consider crude coal tar one of the most valuable drugs in dermatology that I have ever used. I think it is without any doubt the most valuable drug in oozing eczema that I have had occasion to use.

I was astonished, as every one else will be who uses it, at the difference between wood tar and coal tar. No one would dream of using cade oil on an oozing eczema, but the crude tar can be used with certain and often brilliant results. I have not seen a single case of irritation except when I have tried to use it on the scrotum.

In a series of cases of eczema in which the eruption was bilateral, I have used the roentgen ray on one side of the body and crude coal tar on the other and up to the present time I feel that the roentgen ray is more efficient and its action more lasting. The crude coal tar, as a rule, gives the quickest results. It gives almost immediate relief and at the end of a week is generally ahead in its action, but the final results, using it in pure strength, show that the roentgen rays have been more efficacious.

In the future I hope to continue this work and will use the coal tar in the manner suggested by Dr. White.

DR. JOHN E. LANE, New Haven: I first saw crude coal tar used in the Saint Louis Hospital in Paris, where it was frequently applied to the whole surface of the body with a paint brush. For a number of years I have used it extensively, both alone and in various combinations. While different products from different gas works undoubtedly vary to a considerable extent, I have never noticed any marked difference in the action of the different products used. I think Dind of Lausanne and Brocq of Paris were among the first to point out the necessity of "washing" the coal tar to remove excess of alkali. I have found the method for making the *pix carbonis praeparata* of the British Pharmacopoeia perfectly satisfactory for this purpose. The coal tar is placed in a shallow vessel on a water bath at 120 F. for an hour, and frequently stirred.

In applying the coal tar it is most important to apply it as thinly as possible. In cold weather it should be warmed till of the proper consistency, applied as thinly as possible and any excess wiped off with a smooth instrument—a wooden tongue depressor serves well. Talcum powder is dusted over it several times and rubbed in until dry. If this is properly done the coal tar is not dirty, but presents a smooth surface, and makes a better and more lasting covering than collodion.

If used in an ointment this should also be put on very thin and covered with talcum.

Dr. White has called attention to the fact that coal tar should not be mixed with wood tar when a coal tar effect is desired. On the other hand, coal tar is a very useful adjunct to wood tar, and can be mixed with it in preparations in which wood tar is indicated. Its antipruritic action is much greater.

I have found that petrolatum removes coal tar from the skin much more satisfactorily than olive oil. Where a little irritation is not contraindicated, gasoline may be used as a final cleanser.

DR. HOWARD MORROW, San Francisco: I should like to call Dr. White's attention to a very satisfactory way of applying crude coal tar, in Unna's zinc paste, from 2 to 5 per cent. This also can be applied in various forms of dermatoses of the limbs. The preparation can remain on for four or five days and is easily removed and reapplied. We have found it very effective in a great many cases.

DR. CHARLES J. WHITE, Boston (Closing): I am grateful to Dr. Irvine for bringing up the scientific side of the subject, which I did not broach at all. I think he has supplemented the paper in a valuable way.

I have seen only one case of the bullous form which he mentioned. In the Massachusetts General Hospital we once had an epidemic of reactions to the crude coal tar. The patients vomited, had a rise in temperature, showed a widespread, dusky, morbilliform eruption and were distinctly sick people. We finally traced this entirely to the improper mixture of the ingredients. It is very important to get the right crude tar and also to compound it in the right way. The proper method is to mix the crude coal tar and the zinc; then to rub together the cornstarch and the petrolatum; and finally to incorporate thoroughly the two compounds. This method produces a black smooth paste smelling strongly of gas and of tar; the improperly prepared substance is olive green and does not give forth a gassy odor.

PARAPSORIASIS *

ERNEST DWIGHT CHIPMAN, M.D.

SAN FRANCISCO

The group of resistant, maculopapular, scaly erythrodermias comprises erythrodermie pityriasique en plaques disseminées (Brocq), dermatitis psoriasiformis nodularis (Jadassohn), pityriasis lichenoides chronica (Juliusberg), lichenoid psoriasiform exanthem (Neisser) and parakeratosis variegata (Unna, Pollitzer and Santi).

In 1902, Brocq suggested the term parapsoriasis, to include all of these, and differentiated three distinct types: parapsoriasis en gouttes, parapsoriasis lichenoides and parapsoriasis en plaques.

While these three types are alike in histologic architecture, symptomatology and rebelliousness to treatment, they are easily and sharply differentiated on the basis of their respective eruptive elements.

All writers are in accord that the etiology is unknown and that no method of treatment has proved successful.

Having had under recent observation three cases, one of each type, it has seemed worth while to record the case histories, emphasizing what inquiries were entered into with respect to causes and what, if any, therapeutic results were attained.

CASE I.—*History and Examination.*—Miss G., aged 20, a young lady whose activities were largely social, and whose family history was negative, had no disorders of the gastro-intestinal, respiratory, circulatory or nervous system. Neither nutritional disorder nor focal infection was to be found. While certain food proteins had caused local reaction, the withdrawal of the offending food-stuffs had had no influence on the cutaneous disorder.

The first lesions, which appeared two years ago, developed on the chest, axillary folds and abdomen. In character they were papular. Each papule was surmounted with many fine, adherent scales. The progress was intermittent, crops occurring with alternating remissions and exacerbations. A striking feature was the change in character of the lesions. At times they would most closely resemble the medallion-like lesions of pityriasis rosea, while in other exacerbations the picture would strongly suggest lichen planus. In all phases, itching was fairly constant, although never excessive.

Objectively, the lesions were uniform in that they were alike at a given time, although the type varied. Occasionally the papular element was predominant, while at other times scaliness was more pronounced. The lesions were always discrete, with no tendency to grouping. The color varied from a somewhat light café au lait to a fairly pronounced red, although in general

* Read at the Forty-Fourth Annual Session of the American Dermatological Society, at Swampscott, Mass., June 2-4, 1921.

the appearance was only slightly inflammatory. The scales, slightly adherent, were of exceptional fineness, and the underlying surface was dry and of a pinkish tint.

Diagnosis.—Parapsoriasis, lichenoid type was diagnosed.

Treatment.—Various keratolytic agents were for the most part ineffective, although 10 per cent. resorcin paste seemed somewhat to modify the appearance. A few applications of ultraviolet rays, however, caused the lesions to fade away rapidly. Within a few months recurrence was noted. This yielded to the same treatment. In all, three attacks were thus relieved in approximately one year.

CASE 2.—History and Examination.—Mr. B., aged 35, a lawyer, presented a negative family history. The gastro-intestinal system was normal, except for a slight tendency to constipation. The circulatory, genito-urinary and nervous systems were negative and no disturbance of nutrition was found. Intradermal tests with many food proteins were negative. Search for focal infection revealed enlarged and infected tonsils. The general appearance was robust.

The first skin lesions were observed two and one-half years ago. They appeared first on the arms and later on the thighs and legs. The manner of their progress was difficult of appraisal because, once noted, they had apparently attained their full evolution. Thereafter they were subject to slight exacerbations and improvements. Seasonal changes were not noted, but north winds seemed invariably to aggravate the condition. There had been no subjective symptoms. Objectively the lesions were symmetrical in their distribution on the arms, thighs and legs. On the arms the inner aspect was chiefly involved, but the process included portions of both the flexor and the extensor surfaces. On the thighs and legs, the inner aspect was also involved, but the eruption was confined to the extensor surfaces.

At the time of the examination the individual lesion was circular, of the average size of a silver dollar, well defined, showing only the slightest elevation, and no palpable infiltration. It gave the impression of being quite superficial in character. The color may be described as tawny, although there was definite erythema, which at times gave the lesions a predominating pink tone. With a dermal curet, many fine, dry, powdery scales were easily detached, leaving no trace of hemorrhage or moisture of any sort, but a slightly reddened surface.

Diagnosis.—Parapsoriasis en plaques was diagnosed.

Treatment.—On the joint recommendation of the family physician and the laryngologist, the tonsils were removed. Locally a calamin lotion was applied. In two months, there was no change in the appearance of the lesions. The ultraviolet rays were applied in sufficient dosage to cause transient erythema. This caused definite improvement. A second application, in dosage, to produce slight exfoliation, caused practical disappearance of the lesions.

CASE 3.—History.—Mrs. M., aged 26, switchboard operator, gave a family history of no recorded tuberculosis and a tendency toward excessive weight. The mother, two sisters and one brother each weighed over 200 pounds. The father died of locomotor ataxia. In addition to the skin lesions the patient complained of severe bitemporal headaches, poor memory, undue fatigue, excessive drowsiness, irregular menses with tendency toward amenorrhea, sexual frigidity, absence of sweating, overweight and undue sensitiveness to cold.

The eruption began six months ago, appearing first on the arms, then on the hands and the upper portion of the chest, in relatively rapid sequence. Subsequently, it spread over the entire body, a few lesions occurring on the face. The evolution was in general steady without exacerbations or remissions or any changes in the type of lesion.

Examination.—The patient's weight was 242 pounds. There was refractive error but no contraction of the visual fields. The tonsils were moderately enlarged. The axillary hair was scanty. The uterus was infantile. The basal metabolic rate was -25 (three readings); the Wassermann reaction was negative.

Objectively, the lesions were uniform, symmetrically arranged, discrete, scale covered pinkish papules. Although the general appearance was somewhat suggestive of psoriasis or of papulosquamous syphilis, it is to be noted that the scalp, knees and elbows were spared, and the Wassermann reaction was negative. In size there was only slight variation, most of the lesions being somewhat smaller than a split pea. The scales were thick, white, tough in consistence and firmly adherent. On scraping with a dermal curet, a dry, red, nonhemorrhagic surface was exposed.

Diagnosis.—Parapsoriasis, guttate type, was diagnosed.

Treatment.—In view of the physical findings, the following glandular treatment was prescribed: total ovarian substance and corpus luteum, 2.5 grains; thyroid, 0.1 grains; total pituitary substance, 3 grains; one dose four times daily. The refractive error was corrected. Locally, an ointment of salicylic acid, 5 per cent., and oil of cade, 15 per cent., was applied.

After several weeks no improvement was noted, whereupon an ointment of 8 per cent. betanaphthol was substituted for use on the trunk and lower extremities. The arms were treated with ultraviolet rays. While the areas treated with the ointment manifested no improvement, the lesions exposed to the ultraviolet rays responded at once. Following the first application, definite progress was evident. After five treatments, the lesions in the regions exposed to the light had practically resolved. In the meantime, all other local treatment had been discontinued and unmistakable improvement was noted in the remaining lesions, although it was not comparable to that in the regions exposed to the rays.

The response to the internal medication was satisfactory. The tendency to drowsiness and fatigue was greatly ameliorated, the menses appeared at their calculated time, attended with much less nervousness than formerly; the general well-being was marked, and there was a gain in weight of 10 pounds. Because of this last item, the dose of thyroid was increased to 1 grain, four times daily. Two weeks after this change there had been a loss of 3 pounds in weight, and the unresolved lesions of the skin which had been exhibiting some improvement manifested a marked tendency toward recovery. The scaly elements were rapidly disappearing.

CONCLUSION

A review of the facts gathered from a study of these cases will perhaps shed little light on the question of etiology. Two subjects were females; one was a male. All were young and all were robust in appearance. One was sensitized to certain proteins, but the fact seemed unconnected with the cutaneous condition. One had a focal infection,

the removal of which apparently proved it of no etiologic moment. One had endocrine dysfunction which was possibly a contributory factor.

The results of treatment were more positive. In three cases, one of each type, ultraviolet rays caused the disappearance of the lesions to which they were applied. In one case pluriglandular therapy was of undoubted service. The notable improvement which followed an increase in the dosage of thyroid, however, suggests what was probably the most potent endocrine disorder.

ABSTRACT OF DISCUSSION

DR. SIGMUND POLLITZER, New York: A great deal of water has flowed under the dermatologic mill since 1890, when Unna and I published the first case of what is now known as parapsoriasis. I intentionally omit the name of Santi because his case proved subsequently to be one of mycosis fungoides. The difficulty in differentiating between some forms of parapsoriasis and mycosis fungoides, which has since been so frequently mentioned, led to an error in diagnosis even in the first group of cases published.

It is a universal custom to allow the discoverer of a disease to name it, and not to change the name except for some good reason. It seems to me that parakeratosis, which we first proposed, is a far better term than the name now in use, parapsoriasis—a name which is liable to be confusing to the student and which connotes a relationship to psoriasis that does not exist. As a matter of fact, this Association, several years ago, formally adopted the name of parakeratosis as the generic term for this group of cases.

Aside from this undesirable change of name, the years have added nothing to the etiology of the disease, nothing to the histologic picture of the lichenoid type, and has left us, until very recently, ignorant of any methods of successfully treating the disease. Quite recently, a German writer, Hauck, in the *Dermatologische Wochenschrift*, published a series of cases treated with pilocarpin injections, with very remarkable results. Dr. Wise told me a few weeks ago that he had caused the disappearance of the lesions in a case of parapsoriasis by the use of ultraviolet rays. I am sure that he is pleased at the corroboration of his results which Dr. Chipman has given us. If these results should be corroborated in a later series of cases (and I feel that a more extensive series is scarcely necessary, since we already have four cases that have responded promptly), it seems to me we have a valuable method of treatment for parapsoriasis.

The method is valuable even though the affection recurs after a few months, because the application of the ultraviolet light is simple, clean and harmless.

DR. HENRY J. F. WALLHAUSER, Newark: I was extremely interested in the report of Dr. Chipman. I have tried about everything in five cases, without any improvement. One patient, referred to Dr. Wise, improved rapidly under roentgen-ray treatment, but relapsed to the original condition when treatment was discontinued.

DR. FRED WISE, New York: I should like briefly to recount my experience in three cases. The remedy used in these cases by me was roentgen rays. Dr. Wallhauser's case was that of a man with an extensive eruption of parapsoriasis, in whom the employment of sixteen quarter units of roentgen

rays once a week caused a disappearance of the lesions treated. Within two weeks the eruption recurred, just as it was before. I sent him back to Dr. Wallhauser with the request that he treat him with pilocarpin, but I think he did not show up.

The other two cases were of the lichenoid type. The physician who brought them was in the habit of using the ultraviolet ray intensively and extensively, so intensively that after the first treatment the patient usually disappeared. In this case, he gave such an intensive treatment of ultraviolet rays that when the erythema and burning subsided the papules looked as if they had been curetted out. They left a deep depression. The man remained well for a year and then returned with a similar eruption.

The third case was similar, but the lesions were scaly, and the ultraviolet light caused improvement, but produced such bad effects that the patient preferred the disease to the treatment.

I think in all three cases no permanent results were obtained, in spite of Dr. Pollitzer's cheerful outlook.

DR. ERNEST DWIGHT CHIPMAN, San Francisco: I must say I attempted the treatment in these cases with a very doubtful mind. The ultraviolet ray was used rather as a last resort.

The article of the German writer escaped me. I looked in the most recent books available and found no mention of it.

It seems to me Dr. Pollitzer is well within his right in holding out for the title "parakeratosis," but I used "parapsoriasis" because it is the most common term. I agree with Dr. Pollitzer that if we have in the ultraviolet ray a remedy which will do for parapsoriasis what the chrysarobin will do for psoriasis, we have at least gained something in our therapeutic equipment.

HERPES ZOSTER AS A PRIMARY ASCENDING NEURITIS *

DOUGLASS W. MONTGOMERY, M.D.

SAN FRANCISCO

No one now doubts that herpes zoster is a specific microbic disease. Although it is not known to be transmitted from person to person, it occurs in communities in groups of cases at a given time. It has also an almost regular sequential course, an invasion, a status of maintenance and a decrease which take place in a limited period, and its onset and sometimes its status of maintenance are often accompanied by fever. Furthermore, one attack appears to grant immunity, as a second attack is rare. Finally, the characteristic neural lesion on which, since Barensprung's day, the eruption has been conceded to depend, is inflammatory. It is an inflammation of the posterior root ganglion, just such as would be produced by a micro-organism.

THE UNILATERALITY OF HERPES ZOSTER AND ITS LIMITATION TO A REGION

Attention may here be drawn to the fact that only one ganglion, or two at most, and those on one side of the body, are affected. The instances in which more than one ganglion are involved are quite rare, and the cases in which the eruption occurs simultaneously in two widely separated localities, or in which the eruption occurs bilaterally, are so infrequent as to give rise to a question of their being herpes zoster at all.

The situation of the disease, therefore, is one of its most striking features. Where does the virus enter, and by what channels does it attain one, or at most, two ganglions on one side of the body? Does it travel through the blood, or through the lymph vessels, or does it ascend along the affected nerve itself, just as the virus of cerebrospinal meningitis ascends along the olfactory nerve?

It would be very strange indeed if a virus, diffused in the general blood or lymph stream, should hit one ganglion, or at most two, and if it affected two, then that these two should be close together on one side of the body. This might happen in an occasional instance, but it would not happen practically every time, as it does in zoster. It is much more reasonable to suppose that the virus enters the nerve terminals in the skin, and ascends, possibly in the lymph spaces along the nerve sheath, until it strikes the ganglion pertaining to that nerve;

* Read at the Forty-Fourth Annual Session of the American Dermatological Association, Swampscott, Mass., June 2-4, 1921.

and there, finding an exceptionally good culture medium, it grows well and causes an acute inflammation, which in turn causes the eruption of the skin. As neighboring nerves are frequently interwoven, it is not strange that the virus should attain more than one ganglion; but these ganglions are always neighboring ganglions, as they should be.

This is the strongest argument that this paper contains for the maintenance of my thesis, but it is so strong that I cannot see how it can be refuted. There are, however, a great number of facts connected with the disease which fall in most naturally with this main argument.

THE INFLAMMATORY ENGORGEMENT OF THE REGIONAL LYMPHATIC NODULES

Years ago, W. G. Hay, who was then working with me, drew attention to the adenitis which accompanied the onset of herpes zoster. Recently Louis Ramond and Roger Lebel have taken up the same subject, and they accord to it the same importance as to the pains and to the eruption.¹ According to these observers, the lymphatic engorgement is constant, occurring in the most insignificant attacks, is unilateral, and is limited to the glands draining the portion of skin which is to be the seat of the zoster eruption. The swollen gland, for there is usually only one, is never spontaneously painful, but is always tender, and, according to these observers, it clears up spontaneously by the seventh day, while the vesicles and erosions of the zoster are still florescent and undergoing secondary infection. The analogy between this and the other viruses, such as *Spirochaeta pallida*, the streptococcus, the staphylococcus and Ducrey's bacillus, that enter by way of the skin and travel up the lymphatics, is too close to require comment.

That portion of the virus which travels up the main lymphatic stream presumably travels faster than that portion which travels along the nerve, so that the lymphatic ganglion is invaded, inflamed and enlarged before the neural ganglion. The generalized virus is probably the portion which brings about the immunity.

This characteristic adenitis is still another proof that the specific virus of herpes zoster enters on the surface of the skin of the region attacked, and, furthermore, I believe that this enlarged gland, during its primitive enlargement, is the logical place in which to search for the specific micro-organism.

THE PRE-ERUPTIVE NEURALGIAS AND FEVER

For days, and even longer, before the outbreak of the eruption there may be changes in the sensation in the skin in the zoster region,

1. Ramond, Louis, and Lebel, Roger: L'Adenite primitive. Bull. et mém. Soc. méd. d. hôp. de Paris **36**:1157 (Aug. 5) 1920.

such as hyperesthesias, paresthesias, burning, itching and neuralgia-like and rheumatic-like pains. These sensations I ascribe to the effect of the virus on the nerve as it ascends along it. A few days before the zoster eruption there may be a rise of temperature, which falls, however, on the outbreak of the vesicles. It must not be inferred, however, that the temperature drops on account of the outbreak of the eruption; it is rather that at the time the eruption appears the immunity has advanced to a point that permits the temperature to fall to normal; and this is just exactly what one would expect as a result of the action of such a highly immunizing virus as that of herpes zoster appears to be.

IMMUNITY

The immunity conferred by one attack of herpes zoster seems to be almost perfect, as a second attack is almost unknown. This fact is now so generally recognized that the report of an instance in which there is more than one attack gives rise to the suspicion that at least one of them was not true zona. Immunity, I believe, modifies the course of the disease in another important way. The virus enters the nerve by the cutaneous nerve endings, and as almost all these are sensory, the virus almost always enters a sensory nerve. The longer the nerve, the longer the time it would require the virus to reach the ganglion on the posterior or sensory root; and during all this time the patient is being immunized, so that the virus in its journey may die out, and may never attain to this ganglion. Therefore, no zoster eruption may take place, or if the virus does attain the ganglion, the ganglionic inflammation is liable to be very mild, and the eruption correspondingly mild. It may well be that many of the neuralgias of the long nerves are really zoster without zoster eruption.

On the other hand, the shorter the nerve, the shorter the time it will take the virus to attain the ganglion, and the less the immunity, and the severer the inflammation of the ganglion. This would explain the frequent great severity of the zoster eruptions in the area of distribution of the fifth nerve, especially of the very short ophthalmic branch. It would also explain the great variability of intensity of zoster of the body. If the virus enters a nerve near the sternum, for example, it will have quite a long road to travel before it reaches the ganglion, while if it enters a branch farther back, near the vertebral column, it will have a much shorter road and will probably reach the ganglion sooner, and before a good immunization has time to take place.

PREDISPOSING POISONS

In speaking of immunity and its relationships, it may be remarked that certain poisons, such as arsenic, carbon monoxid, arsphenamin, antipyrin and mercury have been observed clinically to predispose to herpes zoster. I have been unable to explain why this should be so.

ZOSTER OF THE TRUNK²

Although 76 per cent. of cases of herpes zoster are of the trunk, Hewlett was able to find only one case in which the muscles were affected, and this would accord with the difficulty the virus would experience in attaining their motor nerves.

ZOSTER OF THE TRUNK²

Zoster attacks of the extremities are rarest of all; but the motor complications are relatively common, and the explanation would be that many of the muscles of the hands and feet are superficially situated, and both, especially those of the hands, are subject to frequent wounds, by which a virus could attain the motor nerves. Motor complications here are only relatively frequent, for, like the attacks in these situations themselves, they are rare.

ZOSTER OPHTHALMICUS

As quoted by Hewlett, Wecker says that ocular paralysis of some sort complicates about 7 per cent. of all cases of zoster ophthalmicus, and the order of the nerves affected is highly interesting. The most frequently affected is the oculomotorius. This might be due to the fact that it is the largest of the three motor nerves of the orbit; but it may also be due to the fact that one of the branches, that supplying the levator palpebrae, is almost a cutaneous nerve, and the others are not far from the free surface. Paralysis of the sixth, or abducens, is more uncommon, and the least common is the trochlear, or fourth, which is situated deeply in the orbit. These motor complications of the third, fourth and sixth nerves are associated with herpes zoster of the ophthalmic branch of the fifth nerve alone. I cannot imagine any virus circulating in the blood that would give rise to these combinations of sensory and motor nerve affections; and I cannot imagine a cause striking a central origin and giving rise to this combination, as there is no center common to the fifth nerve and to the other three.

All these nerves, it is true, pass through the superior orbital fissure and, therefore, in close apposition; but if the symptoms were due to swelling and pressure here, all would be affected, or at least the affection would tend not to be very selective. As a matter of fact, only one or two branches of the sixth nerve may be affected in any one instance. In a case reported by me, a herpes ophthalmicus was followed by paralysis of the corresponding frontalis muscle.³

What has been said of the difficulty of imagining a central origin for those cases of motor paralysis of the third, fourth and sixth cranial

2. I owe almost all the data in this section to the excellent paper of Albion Walter Hewlett, California State J. M., April, 1906.

3. Montgomery, Douglass W.: Zoster Ophthalmicus with Paresis of the Right Frontalis Muscle, Occidental Med. Times 14:109, 1900.

nerves, when combined with zoster of the ophthalmic division of the fifth nerve, applies in a still greater measure to those in which zoster of the cervical nerves is combined with motor paralysis of the seventh cranial nerve. An infection at the peripheral distribution of these nerves could, however, attain both, if introduced into the surface of the skin, for the platysma, a cutaneous muscle of the neck, is supplied by the seventh nerve.

In ordinary palsy of the seventh nerve there is frequently an obtunding of taste in the anterior two thirds of the tongue on the same side. The sense of smell is not affected. Hearing may be altered in certain cases, but Dr. Leo Newmark, who has had a large experience, tells me that, personally, he has never seen it when there were no complications.

In a case of cervical zoster with consecutive paralysis of the facial nerve, recently reported by Pierre Francois Roblin, the paralysis was entirely superficial without causing any trouble of the senses of odor, hearing or taste.⁴ So far, then, as this case is concerned, it contributes its evidence to a peripheral as contrasted with a central affection, and it would be interesting in the future to note whether this is a constant feature. McLeod⁵ mentions a case in which the geniculate ganglion was attacked, but this must be a rare occurrence.

In these motor complications the motor nerves affected are almost invariably on the same side of the body. Not alone this, but they are almost always in the same locality, as, for instance, in ophthalmic zoster the external muscles of the eyeball, or in zoster of either of the other branches, the muscles supplied by the facial. They also occur during the same attack, and these facts would show that they are due to the same infection, taking place at the same time and in the same locality. For reasons hitherto advanced it would seem necessary that this infection take place in the skin.

THE TYPE OF MICRO-ORGANISM INVOLVED

It is probable that the virus often enters by a wound in the skin, and from time to time in the literature one runs across the observation that an injury has been received a short time previously in the affected area, as a zona following a severe contusion of the skull in an automobile accident (Mme. Diondormat-Lempert) and a zona reported as following injury of a nerve branch in giving a mercurial injection (Pollitzer).

As for the type of micro-organism, I think it is a streptococcus, as Rosenow and Oftedal have reported. Directly in line with this is a

4. Roblin, Pierre Francois: *Bull. Soc. franç de dermat. et syph.* (March 11) 1920, p. 113.

5. McLeod, J. M. H.: *Diseases of the Skin*. New York. Paul B. Hoeber, 1921.

clinical observation, accentuated by Thibierge and repeatedly mentioned by other observers, of the occurrence of aberrant vesicles. A scattered vesicular eruption like this is more likely to be streptococcic than anything else. In some rare cases, therefore, a scattered streptococcic eruption may be found on the skin even at the time of the appearance of the true vesicular zona eruption. On the other hand, it is rare for streptococci, no matter of what strain, to cause prolonged immunity, whereas the virus of zoster appears to be highly immunizing.

I would conclude that the zoster eruption is due to a trophic disturbance following inflammation of a posterior root ganglion, and that this ganglionitis is due to a specific virus, possibly one of the streptococci, which attains the ganglion by way of the skin and the peripheral nerves.

ABSTRACT OF DISCUSSION

DR. AUGUST RAVOGLI, Cincinnati: I congratulate Dr. Montgomery on the beautiful paper he has given to us. I want only to remark that the subject was brought up by Kaposi, and he brought out that the cause of the eruption could be found in hemorrhage in the ganglions, in the prevertebral ganglions in which the spinal nerves mix, are separated and then come out as sensitive, motor, trophic, and vasomotor, regulating the sensibility, the motility and the nutrition. When the vasomotor fibers are compressed, together with blisters of the skin, the gangrenous spots occur because the skin is no longer nourished, and when the sensitive axons are compressed, there is terrific pain neuralgia, which precedes, accompanies and follows the zoster eruption. The motor nerves are affected in the same way. Whether there is infection which produces the hemorrhage into the ganglions cannot be established positively. It is usually claimed that zoster is unilateral, but I have had occasion to see cases in which the eruption was bilateral, and in one case I saw two zosteres of the dorsopectoral region on the same side. Hence immunity in these cases would not play a great part. The paper of Dr. Montgomery was instructive and interesting.

Correspondence

USE OF OIL OF ALEURITES TRILOBA OR ALEURITES MOLUCCANA IN THE TREATMENT OF LEPROSY

To the Editor:—I would like very much, as a matter of record, to put before your readers the possibility of the fatty acid derivatives of the oil of *Aleurites triloba* or *A. moluccana*, being of great value in the treatment of leprosy and other skin diseases. The tree is more commonly known as the kukui tree and is distributed throughout Polynesia, the Philippines, India and especially Hawaii.

The fatty acid group of this tree, to my mind, will prove to have equally as good a therapeutic action as that obtained by the fatty acid derivatives of chaulmoogra oil.

I have been able to combine this group of fatty acids with iodine, thus producing an ideal iodine compound which, I believe, may be given subcutaneously or by intramuscular injections.

The oil is obtained from the kukui nut and may be had in sufficient quantity to supply the need of the entire leper world.

JAMES T. WAYSON, M.D., Honolulu, T. H.

Abstracts from Current Literature

A POSSIBLE EXPLANATION OF THE INCREASED INCIDENCE AND EARLY ONSET OF NEUROSYPHILIS. A. REITH FRASER and A. G. B. DUNCAN, *Brit. J. Dermat. & Syph.* **33**:281 (Aug.-Sept.) 1921.

This article, continued from the July number, summarizes the possible explanations of the increased incidence and early onset of neurosyphilis as follows:

1. Neurosyphilis is due to direct arsenical intoxication analogous to the optic atrophy which follows the administration of Fowler's solution.

2. It is due to transient or permanent anatomic damage directly caused by the arsenic.

3. It is an amino-group intoxication.

4. It is a purely syphilitic process (McIntosh and Fildes).

5. It is due to sudden sterilization of the general systemic circulation with resulting paucity of antibody supply, to the cerebrospinal axis. The parasites in the general circulation are killed off and the stimulus for antibody production is thereby removed; this stimulus is not replaced by arsphenamin. The parasites which have invaded the central nervous system are not killed, but are left free from antibody molestation to attack the harboring tissues at will (McDonagh). (This was Ehrlich's suggestion.)

6. It is due to a combination of a purely syphilitic process and an arsenical intoxication accelerated by the traumatic element of postwar neuroses.

The authors feel that the first three theories are untenable, because too little arsphenamin reaches the intrathecal circulation to do serious damage to a healthy central nervous system. That it is a purely syphilitic process seems unlikely, since neurosyphilis was a much less frequent occurrence before the days of arsphenamin. They feel that the most logical explanation is a combination of theories.

Arsphenamin, by killing quickly most, but not all, of the spirochetes, hinders its own ends by hindering instead of furthering the natural supply of antibodies, as it does not itself stimulate their production. It also seems highly probable that the cerebrospinal axis suffers directly or indirectly from the injury of its capillaries as a sequel of the vascular damage by arsenic.

In case of treatment with mercury, if not too severe, the removal of nature's stimulus to antibody formation is slow and never complete, and the nervous system is drawing a supply of antibodies over a long period. When a patient is treated with several successive big doses of arsphenamin, quick sterilization takes place, but if followed for two or three years by continuous small doses of arsphenamin and mercury, the nervous system may be successfully sterilized as well.

Many other factors have to be taken into consideration with regard to the early incidence of nervous syphilis. No two cases of syphilis are exactly alike, and the most important factors which determine the differences are: (1) the patient's resistance, (2) the natural protective power of the central nervous system, (3) the type of infection, (4) the stage at which treatment is inaugurated, and (5) the type of treatment undertaken.

As a result of these observations, the authors suggest treatment of syphilis along the following lines:

"In the early stage every effort should be made to sterilize the host before the stage of generalization has commenced. Vigorous intravenous medication should therefore be carried out. After the generalization stage is in full swing the aim should be to work for a slow, steady and gradual sterilization. Small doses of arsenobenzene at short intervals extended over a very long period will prove the best means to attain this. The nervous system will require all the antibody it can possibly secure, and this circumstance will be defeated if sterilization is sudden and rapid. Intramuscular arsenobenzene, combined with intramine and mercury, is then the best form of treatment."

SENEAR, Chicago.

SYPHILITIC AUTO-INFECTION AND REINFECTION. L. ARZT, Dermat. Wchnschr. **72**:337 (April 30) 1921.

Two cases of apparent auto-infection or reinfection are considered according to Muller's requirements.

CASE 1: A young woman, aged 20, in March, 1918, showed a typical secondary syphilitic eruption and positive Wassermann reaction, with history of illicit intercourse. In February, 1920, after fourteen injections of neo-arsphenamin, clinically and serologically the findings were completely negative. In October, 1920, denying venereal intercourse since February, there appeared a painful swelling of the left inguinal glands and an indolent ulcer on the left labia minora, in which spirochetes were found. The blood Wassermann reaction was negative. On Sept. 4, 1920, the Wassermann reaction became completely positive and on the twentieth of the same month a typical macular, disseminated roseola appeared. An injection of neo-arsphenamin produced a strong Herxheimer reaction.

CASE 2: A woman, aged 29, married, in October, 1919, eight weeks after intercourse with her husband, who had acquired syphilis in the war, presented a grouped, maculopapular eruption, inguinal adenopathy and positive Wassermann test. After thirty mercury and seven arsphenamin injections, the patient received no more treatment and was not seen again until fifteen months later, Feb. 11, 1921, when she presented an indolent sclerotic ulcer, approximately the size of a five-cent piece, on the lower lip and swelling of the submaxillary lymph nodes. Spirochete examination was positive; the Wassermann reaction was negative. In the middle of February a macular exanthem and positive Wassermann reaction appeared. The patient's husband had at this time a syphilitic sore on his lip, as he had received insufficient treatment.

Whether these cases are reinfections with two different strains of *Spirochaeta pallida* or whether the appearance of the second disease-cycle was due to infection with the same strain of spirochetes caused by the first disease-cycle, is difficult to determine. In Case 2, the same person was probably infected twice with the same strain of spirochetes, once genitally and once extragenitally.

ANDREWS, New York.

FORMATION OF NODES IN SCLERODERMA. C. BRUHNS, Arch. f. Dermat. u. Syph. **129**: Pt. 1, 1921.

In rare cases the clinical symptoms of scleroderma show tuberosities of widely differing character. Some patches of circumscribed scleroderma are occasionally seen to rise above the surface of the surrounding skin, themselves showing a distinct sclerotic character with a rough and chopped sur-

face. Of these node-like projections, the surface of which is apparently normal skin, one species consists of deposited calcium salts as shown by the roentgenogram. The other species, however, one example of which the author discusses elaborately, represents, aside from the typically sclerotic skin parts, circumscribed swellings which may be located on the fingers, for example, combined with sclerodactylia, as well as on various parts of the trunk and extremities. Isolated nodules are the rule, though several and even groups sometimes develop. To the touch they are comparatively hard, of the size of a pea and larger, partly confluent, and the skin is firmly adherent to the nodule. The surface is smooth and the color varies from normal to brownish and bluish. Microscopically, they show more or less characteristic changes due to scleroderma, that is, density of the collagenous tissue, also alterations of the vessels. As cases of this kind are so rare in the literature, the author states that further observations are necessary before this new form of "tuberous scleroderma" or "nodular scleroderma" can be sharply defined.

AHLWEDE, Hamburg, Germany.

ROENTGEN-RAY TREATMENT OF ACNE VULGARIS. J. M. MARTIN and C. L. MARTIN. *Am. J. Roentgenol.* **8**:468, 1921.

The autocontrolled transformer and a broad focus Coolidge tube were adopted for use with the following factors: (1) a 5-inch spark gap; (2) five milliamperes; (3) target distance of 2 inches; (4) an exposure time of from three to five minutes, and (5) a filter of 5 mm. of aluminum placed just beneath the tube and a piece of leather placed directly over the area exposed. A single exposure of 25 milliamperes will produce a mild degree of reaction in the average skin. The exposure should under no circumstances be repeated in less than a week. Dosage obtained by factor determination has been found most reliable.

A report of changes in sebaceous glands after roentgen ray is given. The skin was that of white guinea-pigs. The chief changes noted were a thickening and desquamation of the horny layer, a flattening out of the sulci and papilli; a gradual shrinking of the hair follicles with loss of hair shafts; a marked thickening of the collagen bundles of the corium, and a disappearance of the sebaceous glands at about the time that the hair follicles begin to shrink. At the end of eight days after an exposure of forty-five minutes, 2½-inch parallel spark gap and 10 milliamperes there are a few such glands in the exposed area, and an occasional one may be observed in the ten-day section. In the section twelve days after exposure no glands were found. If the sebaceous glands are the seats of infection in acne, as many believe, it seems reasonable that destruction of such glands by roentgen ray should effect a cure.

Human skin was not studied.

GOODMAN, New York.

ARSENIC FOUND MICROCHEMICALLY AND HISTOLOGICALLY IN A CASE OF HYPERKERATOSIS ARSENICALIS. R. BRUNAUER. *Arch. f. Dermat. u. Syph.* **129**, Pt. 1, 1921.

A female patient developed symptoms of hyperkeratosis arsenicalis palmaris et plantaris after eighteen months' administration of solution of potassium arsenite (Fowler's solution) per os. In a piece of hyperkeratotic skin which was dissected, a sulphur arsenic compound—arsenotrisulfid—was found by a special method of preparation based on the chemical qualities of this compound. A

deposit of distinct yellowish coloring was seen. The probability that this deposit consisted of arsenotrisulfid was strengthened by the fact that the urine of the patient also contained arsenic, while a piece of skin from a hyperkeratotic process of different etiology, which was used as a control and treated the same way, gave negative results. The arsenosulfid is abundant in the rete malpighii, in the sweat glands and in the nerves. Smaller quantities are found in the stratum corneum, in the vessels of the papillary body and in the sub-papillary rete. The distribution of the arsenotrisulfid supports the theory of those authors who hold that hyperhidrosis is a necessary symptom of arsenokeratosis and of those who describe the keratoses as located around the orifices of the sweat glands, also of those observers who hold that hyperkeratotic processes take their origin from the orifices of the sweat glands.

AHLWEDE, Hamburg, Germany.

ERYTHEMA NODOSUM LUETICUM (SPIROCHETES AND HISTOLOGY). F. FISCHL, Arch. f. Dermat. u. Syph. **129**: Pt. 1, 1921.

The finding of *Spirochæta pallida* in erythema nodosum, as well as the prompt response of this condition to antisiphilic treatment proves that the nodules represent specific manifestations of syphilis. Therefore an erythema nodosum lueticum really exists. Syphilis here again imitates other dermatoses, as it does in the psoriatic syphilids, in lichen siphiliticus and clavus siphiliticus, etc.

AHLWEDE, Hamburg, Germany.

THE RELATION OF LUPUS ERYTHEMATODES TO TUBERCULOSIS. AAGE FOENNS, Arch. f. Dermat. u. Syph. **129**, Pt. 1, 1921.

The investigations of Bloch, Fuchs and Bruusgaard in a few cases made the tuberculous origin of the lupus erythematodes highly probable. The author adds two other cases which support the relation of lupus erythematodes to tuberculosis. In by far the larger number of cases, however, the tuberculous origin cannot be traced. Important facts, such as the negative influence of tuberculin on lupus erythematodes, rather show that a causative relation between the two conditions is not probable.

AHLWEDE, Hamburg, Germany.

THE PREVENTIVE AND CURATIVE TREATMENT OF THE NITRID CRISIS. G. MILIAN, Presse méd. **65**:643 (Aug.) 1921.

The author discusses in chronologic order the prophylaxis of the products most apt to cause and the medical and curative treatment of the nitritoid crisis. Under prophylaxis he emphasizes the desirability of injecting a dilute rather than a concentrated solution of any of the arsphenamin products. He states that if one is susceptible to the nitritoid crisis, it may be provoked more easily and more seriously with a concentrated solution; but if one uses a dilute solution, a few cubic centimeters may be introduced intravenously; a few minutes should be allowed to elapse before the remainder of the solution is allowed to flow into the vein. Should any of the premonitory symptoms of the nitritoid crisis be noted one can easily discontinue the injection before it has become well established. He rejects promptly the acid salt of arsphenamin; the too highly alkalinized preparation; neo-arsphenamin which has been allowed to stand too long, and "certain lots" of the so-called "914," all of which may produce the nitritoid crisis.

The medical and curative treatment which he strongly advises is epinephrin hydrochlorid. He believes that the syphilographer of the present day should have ready a sterile syringe containing 1.5 mg. of epinephrin. Should the patient show any of the characteristic signs of a nitritoid crisis, one should immediately inject intramuscularly the solution mentioned. In this way serious results may be averted.

McCAFFERTY, New York.

THE X-RAY IN DERMATOLOGY. C. GUY LANE, *Am. J. Roentgenol.* 8:476, 1921.

A report is briefly made of the activities of the roentgen-ray department of the Massachusetts General Hospital. From October, 1919, to April 1, 1921, the total number of treatments for cutaneous conditions have been 656. Ringworm has responded more satisfactorily to roentgen-ray treatment than to any other form of treatment. Good results were obtained with only 70-80 per cent. epilation in few cases, early in the standardization of the technic, in which after-treatment has been carried out satisfactorily. Epithelioma requires thorough curetting of the lesions to have the number of exposures lessened. Dosage should be nearer twice an erythema dose, unfiltered, to obtain the most satisfactory results. Patients with neurodermite cases have without exception become well with fractional, unfiltered doses administered once a week or once in two weeks. In mycosis fungoides, roentgen-ray treatment has aided the involution of the lesions and relieved the intense itching. A cure is not expected with this treatment. The majority of patients with chronic eczema cases have been relieved. One patient with blastomycosis made satisfactory progress after roentgen-ray treatment was instituted in addition to internal administration of potassium iodid. In pruritus, roentgen-ray treatment was the court of last resort, and the results have been surprisingly good.

In the following diseases the results were only fair: acne, tuberculosis of the skin, favus, keloid, acne keloid and parasitic diseases of the skin, referring to certain probable ringworm affections of the hands and feet, although the organisms were not demonstrated.

Results have been unsatisfactory in: sycosis, lupus vulgaris, urticaria, hyperhidrosis and psoriasis.

GOODMAN, New York.

THE FLOCCULATION REACTION OF SACHS-GEORGI AND MEINICKE IN THE SERODIAGNOSIS OF SYPHILIS. W. GAHTJENS, *Arch. f. Dermat. u. Syph.* 129: Pt. 2, 1921.

These reactions are simple and specific for syphilis. Both methods are a little less sensitive than the Wassermann reaction; they cannot be substituted for it, but they are a valuable support. Comparison of the two shows that the same results are attained in 95 per cent. of the cases. The Sachs-Georgi reaction has not been found superior to the Meinicke. If the quantitative conditions are considered, the Meinicke reaction is more sensitive, as the maximum of flocculation is more frequent; on the other hand the Sachs-Georgi reaction is more efficient in quality and more frequently shows positive results than the Meinicke in cases which are Wassermann negative. The observation time of forty-eight hours has the advantage of distinctly strengthening weak positive and doubtful results. The duration of both reactions may be considerably shortened by half an hour of centrifuging.

AHLWEDE, Hamburg, Germany.

THE TREATMENT OF CHRONIC TUBERCULOSIS BY THE SULPHATES OF THE RARE EARTHS. GRENET and DROUIN, *Bull. méd. de Quebec* **6**, 7, 8: (Feb., March, April) 1921.

The experiments of Frouin appear to have shown that the salts of the rare earths (sulphates of cerium, yttrium, scandium, etc.) destroy the bacillus of tuberculosis in vitro, and that their intravenous injection gives rise to a temporary leukocytosis. So the authors employed the sulphate in 2:100 aqueous solution intravenously or in 2:1,000 oily solution intramuscularly or subcutaneously, the injections of 0.1 grain being given every day or every other day for an average series of twenty, with an average interval of twenty days between series. Other modes of administration had been tried and found to be inferior. It is emphasized that only chronic, afebrile forms of the disease can safely be treated thus, the therapy being contraindicated in acute cachectic or febrile cases.

The results are recorded, and in all forms of tuberculous involvement they are encouraging. The tuberculids also responded well, especially lupus erythematosus, acnitis and erythema induratum. In tuberculosis verrucosa cutis and in lupus vulgaris it is well to combine treatment by scarification with these injections, several series of which may be required, and even a year's treatment, to effect a cure. Other tuberculous nodules and ulcers respond slowly to the treatment. Tuberculous adenitis and the resultant sinuses usually heal rapidly. In any case, however, several series may be required to gain a cure, and we are cautioned against hastily pronouncing the treatment ineffective.

PARKHURST, New York.

THE VARIOUS RESULTS OF RESEARCH WORK ON SYPHILIS. F. FRÜHWALD, *Arch. f. Dermat. u. Syph.* **129**: Pt. 2, 1921.

In 1904, Hallopeau fixed a program for research work on syphilis, most of the questions of which can be answered now. 1. In which stage of the disease is the blood infectious? Spirochetes may circulate in the blood at any time. 2. When does the virus enter into the system? In the fifth or sixth week following the infection, probably earlier. 3. Does the virus penetrate into the system only a few days before the appearance of the secondary symptoms? Approximately three weeks after the infection the sclerosis appears. Three weeks later there is an exanthem. 4. Is the sperm in the stage of generalization inoculable? Finger, Landstein, Uhlenhut and Mulzer say yes. 5. Are the tertiary products infectious? Yes. 6. Is it possible to isolate from the body of a syphilitic a substance similar to "tuberculin"? Neisser's experiments to gain a syphilis vaccine from monkeys failed.

AHLSEDE, Hamburg, Germany.

A CONTRIBUTION TO THE KNOWLEDGE OF THE PHYSIOLOGY OF THE SYMPATHETIC NERVES OF THE SKIN. A. BUSCHKE and E. SKLARZ, *Dermat. Wchnschr.* **72**:235 (March 26) 1921.

To determine the relation of the vasomotor nerves of the skin to nevus anaemicus and vascular nevi, numerous experiments were undertaken, in which epinephrin was used intracutaneously. Injections were carefully made, using 0.2 c.c. of a 1:1,000 solution, with a control of physiologic saline solution. All areas of the body reacted similarly; one-half to one minute after the injection an

anemia appeared; the skin about the blister became bluish-white and the hair follicles stood in erection—a true local gooseflesh. In syphilis the roseola was not always dissipated, but papular syphiloderms were blanched so that the brownish pigmentation became strongly evident. Even more pronounced was this reaction in tertiary tuberculous syphiloderms. Lupus vulgaris, psoriasis, erythema nodosum, erythema exudativum multiforme, urticaria factitia, and pemphigus showed practically no effects from the injections. In vitiligo the erection of the hairs was extremely evident. Several telangiectatic nevi were investigated. The smaller of these became contracted, whereas the larger were only slightly influenced. In pigmented nevi the anemia produced caused relative hyperpigmentation. In alopecia areata the results were inconclusive.

ANDREWS, New York.

CURIOUS LOCATION OF A SKIN DISORDER CAUSED BY INTRA-PERITONEAL INJECTION OF A POLYPEPTID. ABDERHALDEN and WEIL, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Various peptids were injected into the peritoneum of guinea-pigs. Following the injection of a heptapeptid—hexaglycin-glycin—the skin on the back of the animals on both sides of the spinal column showed distinct reddening. Two days later scabs were formed and followed by loss of hair and complete peeling of the skin. Ten days later the hair began to grow, the bald areas being covered with hair. This effect was attained regularly by intraperitoneal injections; the polypeptid had no effect when administered subcutaneously. The authors believe that the nervus sympathicus is irritated and damage caused to these centers. He refers to Unna who called attention to the connection between the various areas of the skin and the nervous system.

AHLSEWEDE, Hamburg, Germany.

CONCERNING THE REPORTS OF ALOPECIA AREATA AND OF SYPHILIS, ESPECIALLY HEREDITARY. R. SABOURAUD, Presse méd. **59**:581 (July) 1921.

The author believes that there is only one true syphilitic alopecia, and it is the one accompanying secondary syphilis. He states that the fingernail sized areas of alopecia occurring especially over the temples and occipital regions may possibly be accounted for by the preexistence of maculopapules just prior to the characteristic alopecia. This syphilitic alopecia differs from the other postinfectious alopecias only by its characteristic spotted appearance.

He discusses at some length the pelade of the French or alopecia areata of Americans. He believes that patients with old acquired and hereditary syphilis give a larger percentage of alopecia areata. He supports these contentions to some extent by referring to the statistics of Fournier and others, who have found certain physical abnormalities associated with alopecia areata. This was especially true of children who presented one or more definite physical malformations with an associated alopecia areata which quickly cleared up in several instances under antisymphilitic treatment.

There is not much mention made of the serum reaction in these cases. He concludes, however, by stating that he does not wish to give the impression that the etiology of alopecia areata is syphilis, but that one must always rule it out as a possible etiologic factor.

McCAFFERTY, New York.

CARCINOMA CUTIS IN AN ANTHRACENE FACTORY. W. J. O'DONOVAN, *Brit. J. Dermat.* **33**:291 (Aug.-Sept.) 1921.

Reporting three cases of carcinoma cutis of the squamous and horny cell type occurring among workers in an anthracene factory, O'Donovan finds:

1. Elderly anthracene workers are liable to carcinoma of the skin similar to those found in sweeps, tar, creosote and paraffin workers.
2. These growths are squamous and horny-celled carcinomas; metastases have not been found.
3. Unlike tar cases a multiplicity of growths in any one patient was not encountered. Four years was the longest and three months the shortest duration of the growths.
4. Minor lesions, acne, keratoses, telangiectases and pigmentation, are common features in workers on the plant.
5. A plant may run for thirty-five years before a carcinoma case develops.
6. The handling of purified anthracene does not appear to be accompanied by the industrial hazard attributed to the handling of anthracene cake.

SENEAR, Chicago.

PRIMARY SPONTANEOUS SQUAMOUS CELL CARCINOMA IN MICE. MAUD SLYE, HARRIETTE F. HOLMES and H. GIDEON WELLS, *J. Cancer Res.* **6**:57 (Jan.) 1921.

In 28,000 consecutive necropsies on mice, demonstrating about 4,000 primary spontaneous tumors, there were only 152 primary squamous or stratified malignant epithelial neoplasms of which seventy were squamous cell carcinoma of the skin and mouth and fifteen basal cell carcinoma of the skin. All of the basal cell and all but sixteen of the squamous cell lesions were located on the head and neck, parts exposed to frequent traumatism, especially in cage animals. A chronic, apparently traumatic, dermatitis preceded many of the face lesions; mouth lesions were associated with bad teeth, and most of the trunk lesions as well as many on the face were located at the sites of healed wounds. Most all lesions occurred in late middle life or old age. In microscopic features the lesions did not differ from those of the same type occurring in man, but a striking absence of lymphatic metastases was observed in mice. The comparative rarity of epithelioma in rats, in view of the great frequency of parasitic skin infections with papillomatous epithelial overgrowths was noted.

H. R. FOERSTER, Milwaukee.

HISTOLOGIC EXAMINATION OF MERCURIC SKIN ALTERATIONS. J. ALMKVIST, *Arch. f. Dermat. u. Syph.* **129**: Pt. 2, 1921.

Minute histologic investigation of mercuric exanthemas (dermatitis following the administration of mercury) showed that in these cases the skin suffers chiefly in two respects: (1) by dilatation of the vessels and edema formation and (2) by the development of bacteria. The former is due to the toxic effect of mercury, probably the effect on the sympathetic nerve, the increase of bacteria being a consequence of the better soil the edema causes.

AHLSEWEDE, Hamburg, Germany.

EXPERIMENTAL INOCULATIONS IN SCARLET FEVER. G. F. DICK and G. H. DICK, J. A. M. A. **77**:782 (Sept. 3) 1921.

Experiments were conducted on volunteers who had never had scarlet fever. Negative results were recorded when blood serum from scarlet fever patients was swabbed on the tonsils of four subjects, and when serum and whole blood were injected subcutaneously.

Mucus from the throats of early cases, filtered through Maasen or Berkefeld N filters and then swabbed on the tonsils of fifteen volunteers also gave negative results. Subcutaneous injections of the mucous filtrate were likewise without result.

Complement-fixation tests with twenty-six bacterial antigens (organisms obtained from the throats of scarlet fever patients) were inconclusive.

Pure cultures of a hemolytic streptococcus obtained from the throats of scarlet fever patients were swabbed on the throats of thirty-six volunteers. Twenty-three volunteers remained free from symptoms; seven developed sore throat, fever and leukocytosis, but no skin rash.

A pleomorphic organism found in the throats of scarlet fever patients was obtained in pure culture and swabbed on the throats of nine volunteers; seven showed no effects; two developed sore throats, fever and leukocytosis, but no skin rash.

In these experiments, no instance of typical scarlet fever was produced.

MICHAEL, Houston, Texas.

VITILIGO OF THE LUMBAR REGIONS. K. KREIBICH, Dermat. Wchnschr. **72**:178 (March 5) 1921.

A case of band-like vitiligo of the lumbar regions, illustrated by photographs, is described. The depigmentation conforms to the areas of greatest pressure from clothing. Histologically only pigment changes exist.

Some persons have a decreased resistance of the skin to pressure. Von Hanawa and von Koenigstein have confirmed this view by demonstrating a diminution of tactile, pain and temperature sense in vitiligo. It is only a step further from this reduced sensibility to diminished trophism, a lessened cell metabolism and diminished pigment production.

Hyperpigmentation is a more frequent sequel to pressure than vitiligo, especially in brunettes, as seen frequently on the lateral lumbar regions with lichenification or over the seventh cervical spine. If the pressure is marked, the pigment loss may not be vitiligo, but a loss of pigment in atrophy following a traumatic erythema.

ANDREWS, New York.

A CASE OF POIKILODERMA ATROPHICANS VASCULARIS. BETTMANN, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

The author mentions a case the clinical and histologic symptoms of which correspond to those of poikiloderma atrophicans vascularis first described by Jacobi. This condition causes atrophy, pigmentation and angiectasis such as are seen in scleroderma and lupus erythematoses. An exact definition and classification is difficult, owing to the small number of cases which have come under observation.

AHLWEDE, Hamburg, Germany.

UNNA'S "BALLOON DEGENERATION" OF THE PRICKLE CELLS
IN THE LIGHT OF RECENT INVESTIGATIONS. B. LIPSCHUETZ.
Dermat. Wehnschr. **72**:340 (April 30) 1921.

The demonstration of "balloon degeneration" by Unna spanned the bridge from the herpes group (herpes zoster, herpes genitalis, herpes febrilis) to the pox group (variola, varicella). Of the four changes defined by him—the rounding off and loss of the prickles, the chemical change of protoplasm leading to a plastic or doughy consistency, and finally the nuclear changes—we are especially interested in the last. According to Unna, the nucleus swells and loses its normal chromatin network so that the chromatin is assembled more at the periphery of the nucleus, where it begins to divide and undergo amitosis. At this stage cells with from two to thirty-two nuclei, which may be basophilic or acidophilic, appear. The subdivided nuclei remain closely pressed together, often as facets.

Researches by the author on rabbits have led to the conclusions that balloon degeneration of the prickle cells is a reaction toward a dermatropic virus and that this is of the Chlamydozoa or Strongyloplasmata. Injections of the vesicular contents of herpes genitalis into a rabbit's eye produced keratitis herpetica, and similar injections into rabbits' skin caused "balloon degeneration." The nuclear inclusion bodies are probably stages in the life cycle of a dermatropic virus.

ANDREWS, New York.

NEURORECURRENCES IN SYPHILIS WITH SPECIAL REGARD TO
TREATMENT WITH ARSPHENAMIN. H. BRÜNING, Arch. f. Dermat.
u. Syph. **129**: Pt. 2, 1921.

Neurorecurrences are syphilitic disturbances of the central nervous system in the early secondary stage of syphilis. Specific antisiphilitic treatment cannot always prevent their development. Statistics show that they were as frequent in pre-arsphenamin times as now. Neurorecurrences are not due to arsphenamin poisoning. The basis is always syphilis wherever latent foci suddenly flare up. Careful dosage of arsphenamin may prevent neurorecurrences; often complete cures are effected.

AHLWEDE, Hamburg, Germany.

CURIOUS FORMATION OF CORNEOUS CYSTS COMBINED WITH
TUBERCULOSIS CUTIS. H. BRÜTT, Arch. f. Dermat. u. Syph. **129**:
Pt. 2, 1921.

This article deals with the formation of extensive corneous cysts showing distinct relation to tuberculosis cutis.

AHLWEDE, Hamburg, Ger.

A CONTRIBUTION TO OUR KNOWLEDGE OF TUBERCULOID
LEPROSY. E. BRUUSGAARD, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

A case of leprosy is described, the clinical symptoms of which resemble tuberculosis. Tuberculoid leprosy is probably that form of the disorder in which the strong defensive action of the system overcomes the infection more easily than in the maculo-anesthetic form.

AHLWEDE, Hamburg, Germany.

EFFECT OF A REDUCTION OF LYMPHOCYTES ON THE GROWTH RATE OF TRANSPLANTED SPONTANEOUS TUMORS IN MICE. FREDERICK PRIME, J. Cancer Res. **6**:1 (Jan.) 1921.

Using more than 2,100 animals and employing Murphy's technic for reducing the lymphocytes, the author demonstrated that reducing the lymphocytes by small doses of roentgen rays does not render mice more susceptible to the inoculation of spontaneous tumors from mice of the same strain; also that spontaneous lymphocytosis does not increase the resistance to the implantation of such tumors.

H. R. FOERSTER, Milwaukee.

FURTHER INVESTIGATIONS OF METASTATIC DERMATOSES IN GENERAL ACUTE BACTERIAL DISORDERS. E. FRAENKEL, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

In meningitis and pneumonia, extravasation of blood into the skin is possible. Though macroscopically the appearance is the same, histologic examination reveals great differences. Meningococcic meningitis may cause inflammation, in serious cases accompanied by necrosis of the collagenous tissue. In the Friedländer meningitis the hemorrhages are inflammatory alterations of the vessels of the subcutis due to the bacilli of the Friedländer group.

AHLSWEDE, Hamburg, Germany.

STANDARDIZATION OF THE WASSERMANN REACTION. J. A. KOLMER, J. A. M. A. **77**:776 (Sept. 3) 1921.

Kolmer calls attention to the well-known drawbacks of the Wassermann reaction, both of the original technic and of the many variations which have been proposed. Believing that it was eminently desirable to develop a standardized Wassermann reaction, he has studied every phase of the test, and as a result of this intensive investigation proposes a new method which he hopes will be given a thorough trial by serologists and adopted as a standard technic if it proves its value.

The present article does not give the details of the test (this is to be published in the *American Journal of Syphilis*) but indicates, in some detail, the principles that have been adopted to make the test better than any of those in use.

The proposed technic, it is asserted, meets the requirements of high sensitivity, practical specificity, technical accuracy and uniformity in results, furnishes a quantitative reaction, and at the same time is relatively simple and economical.

MICHAEL, Houston, Texas.

CONTRIBUTIONS TO THE PATHOGENESIS OF THE SOFT CHANCRE. C. BRUCK, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Soft chancre represented from 10 to 15 per cent. of all venereal diseases among the German soldiers of the west front. The author mentions two cases of women infecting soldiers with ulcer molle without themselves showing any clinical symptoms of soft chancre. Statistics show that a maximum of soft chancre cases is attained during hot weather, the minimum during the months of cold weather.

AHLSWEDE, Hamburg, Germany.

DISCIFORM KERATITIS SECONDARY TO SMALLPOX. HARVEY K. FLECK, Am. J. Ophth. **4**: No. 8 (Aug.) 1921.

This article contains a report of a case and a review of the literature.

Disciform keratitis is a keratitis that consists in the development of a gray disk-shaped opacity in the middle layers of the cornea, due to infection of the cornea from without, usually following traumatism. In smallpox this condition usually occurs in the third week of the disease after desiccation has commenced. Smallpox pustules do not form on the cornea.

H. R. FOERSTER, Milwaukee.

MATCHBOX DERMATITIS. M. FREI, Med. Klin., No. 16, 1921.

Several cases of dermatitis were seen at the Jadassohn clinic, undoubtedly due to matchboxes. The lesions were in the pocket area, also on the hands and face. The causative factor was a phosphorous sulphur compound which was traced to one special factory. Investigation proved that owing to a shortage of amorphous phosphorus a substitute (phosphoresquisulfid) had been used. A certain predisposition of the patient seems to be necessary. Similar cases have been seen in Sweden and Denmark.

AHLWEDE, Hamburg, Germany.

WHAT IS THE BEST TREATMENT OF SYPHILIS? A. BRISO, Gac. Med. Mexico **1**:531, 1920.

The author outlines the general treatment of syphilis and insists on mercury as the basic drug. He discusses in detail the advantages and disadvantages of arsphenamin, mercury and the iodids. He speaks highly of the American arsphenamin (D. R. L.) and criticizes the tendency of the Mexican public to exact from the physicians the genuine German product. He speaks enthusiastically of the intraspinal treatment of neurosyphilis. The article is a general survey of the therapy of syphilis.

PARDO-CASTELLO, Havana.

DIFFERENTIATION OF TYPE OF BACILLUS IN TUBERCULOSIS CUTIS WITH SPECIAL REGARD TO LUPUS VULGARIS. W. ANDERSEN, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Attempts were made to differentiate the "typus humanus" and the "typus bovinus." Thorough investigation of lupus vulgaris in twenty-nine patients, only succeeded in definitely fixing three cases as caused by *Typus bovinus*; the rest were due to *Typus humanus*.

AHLWEDE, Hamburg, Germany.

INFLUENCE OF THE LYMPHOCYTE ON THE PERITONEAL IMPLANTATION OF SARCOMA IN MICE. ELLIS KELLERT, J. Cancer Res. **6**:41 (Jan.) 1921.

Studies in white mice on the lymphocyte content of the peritoneum, which is rich in cellular elements of which 55 per cent. are lymphocytes, failed to show any cellular changes following successful inoculation with mouse tumor implants, or any direct antagonistic actions between the lymphocytes and the tumor implants.

H. R. FOERSTER, Milwaukee.

TREATMENT OF SYCOSIS BARBAE (WITH SPECIAL REFERENCE TO THE TURPENTINE PITCH OINTMENT). L. FREUND, Arch. i. Dermat. u. Syph. **129**: Pt. 1, 1921.

The author speaks highly of the following method of treating sycosis barbae: The diseased area is first exposed to a full Sabouraud pastille dose (hard tube 5-6 benoist walther). Following the epilation the bald area is well rubbed twice, a day during the course of five to six weeks with the following ointment: Pure rectified oil of turpentine, tar (picis liquidae), each 2.5 parts; petrolatum, 50 parts. Roentgen-ray epilation is essential. The ointment prevents recurrence. Deep suppuration requires surgical treatment.

AHLSEWEDE, Hamburg, Germany.

EXPERIENCES IN TREATMENT OF VENEREAL WARTS WITH ROENTGEN RAYS. F. MATT, München. med. Wchnschr., No. 22, 1921.

A 0.25 zinc screen is recommended. Wide broad areas of the lesion are more suitable for this kind of treatment than circumscribed small patches.

AHLSEWEDE, Hamburg, Germany.

THE PATHOLOGY OF PSORIASIS. R. WAGNER, Dermat. Wchnschr. **72**: 193 (March 12) 1921.

Two cases of psoriasis occurring after attacks of impetigo in anemic nervous children are described. In one instance the eruption was linear extending down the left thigh. It remained localized in the third and fourth lumbar segments for two years, although not definitely along the line of any major nerve or metamere.

Hebra mentions the association of neuralgia and sciatica with psoriasis. Weyl states that there is a functional weakness of the nervous center regulating the nourishment of the skin. Polotebnoff concludes that psoriasis is only a symptom of a vasomotor neurosis. In spite of the many other theories concerning the origin of this disease, the neuropathic theory today holds a superior position. In recent literature trauma is frequently an exciting factor. Cases have been reported after bullet wounds and painful compression of nerves by scar tissue. Dreams have preceded the onset in many instances.

ANDREWS, New York.

TREATMENT AND ETIOLOGY OF CHRONIC ECZEMAS. HILGERMANN, München. med. Wchnschr. **68**:702, 1921.

Eczema is a parasitic disease. It is caused by various bacteria and fungi living in symbiosis. These were cultivated by the author under strict asepsis and vaccines prepared. Chronic eczemas, which had persisted for years, were cured in a few months. Treatment is begun with small doses. The second injection is not made before the reaction of the skin and the neighboring glands has died down. It is all important to continue this vaccine therapy long enough, that is, after eczema has disappeared.

AHLSEWEDE, Hamburg, Germany.

A CASE OF BILATERAL HERPES ZOSTER OCCIPITALIS. W. TREUHERZ, Dermat. Wchnschr. **72**:243 (March 26) 1921.

The unusual rarity of bilateral herpes zoster is recognized by most authorities. The writer describes a typical case involving areas supplied by the

second and third cervical nerves. The onset was preceded by pain in the occipital region. The following day a grouped vesicular eruption appeared to the right of the midline in this area, and subsequently groups of vesicles erupted behind the left ear. According to many authors, the incidence of herpes zoster is seasonal. In the spring or fall the disease is most prevalent.

ANDREWS, New York.

TREATMENT OF CALLOUS ANAL ECZEMA. M. BOCKHART, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Three to four times a day alcohol is applied to the area, then a lotion (zinc oxid, talcum, glycerin, water equal parts) until itching and inflammation cease. From eight to ten days later a 5 per cent. liquor picis carbonis in increasing doses is applied. During the whole course of treatment the disinfection and degressing with alcohol must be done three times a day.

AHLWEDE, Hamburg, Germany.

THE SYPHILITIC CRY. S. RAMIREZ, Gac. Med. Mexico **1**:474, 1920.

Ramirez reports several cases of heredosyphilitic children without apparent clinical symptoms, who immediately or shortly after birth presented the peculiar, constant, high-pitched cry described for the first time by Sisto of Argentina. He thinks the cry is due in most cases to the pain caused by the inflammation of the conjugal cartilage of the long bones (epiphysitis).

PARDO-CASTELLO, Havana.

A CASE OF LIQUOR SYPHILIS (NAST) WITH ANATOMIC ALTERATIONS OF THE CENTRAL NERVOUS SYSTEM. E. DELBANCO and A. JAKOB, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

A syphilitic patient without clinical symptoms showed a positive spinal fluid reaction. The only affection of the central nervous system found were isolated tender infiltrations of the meninges cerebri and of the spinal cord, which must be considered specific.

AHLWEDE, Hamburg, Germany.

PSORIASIS ARTHROPATHICA (INCLUDING THE SO-CALLED "HYPERKERATOTIC EXANTHEMATA" IN GONORRHEAL JOINT AFFECTIONS). A. FALK, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

The author proves that a special joint disorder is out of the question in psoriasis arthropathica. This is a psoriasis which by some simultaneous joint affection is strongly influenced in its course, character and location.

AHLWEDE, Hamburg, Germany.

A CASE OF PAPILLOMATOSIS CUTIS. G. FANTL, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

This is the second case of the disease described by Vollmer in 1906. The condition consists of a new growth of unknown etiology which the author distinguishes histologically and clinically from similar papillomatous growths, especially from cases of excessive warts.

AHLWEDE, Hamburg, Germany.

ABORTIVE TREATMENT AND REINFECTION. E. FINGER, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

The success and failure of treatment depends on a third factor which cannot be influenced, that is, on the cooperation of the body of the patient, a factor without which our medication would be ineffective.

AHLWEDE, Hamburg, Germany.

THE PROPORTION OF THE EXTRAGENITAL INITIAL SCLEROSES TO THE SPREADING OF SYPHILIS. W. F. SCHER, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

The author calls attention to the increasing number of extragenital syphilitic infections in Germany, the chief cause being the ignorance of the danger and the contagiousness of the disease among the laity. The demobilization of the army with its utter lack of sanitary prophylaxis accounts for the enormous increase of the infections in this respect.

AHLWEDE, Hamburg, Germany.

SPOROTRICHOSIS IN MEDICINE. LANGLAIS, Bull. méd. de Quebec **8**: 225 (April) 1921.

A historical sketch is given and a description of the various manifestations of the affection, with methods of diagnosis and treatment. The cultural method of diagnosis is recommended and carefully described.

A fatal case seen lately by the author is briefly recorded. In a girl of 3 years the nodules were disseminated generally, and after nearly two years of treatment with iodids by mouth, a terminal pulmonic involvement ensued.

PARKHURST, New York.

THE ETIOLOGY OF LICHEN RUBER. E. GALEWSKY, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Twenty-six cases of lichen ruber among relatives have been published. This number is too small to furnish proof of the parasitic nature of the lichen. The fact that in ten families both parents and children had lichen seems to show that the disease is hereditary. Immunity against lichen does not exist. Galewsky mentions cases in which irritation (vaccines, trauma, sunlight) caused a fresh outburst of the disease.

AHLWEDE, Hamburg, Germany.

THE TREATMENT OF LUPUS ERYTHEMATOSUS WITH CARBON DIOXID SNOW. J. GONZALEZ URUEÑA, Gac. Med. Mexico **1**:424, 1920.

The author relates the wonderful results obtained by him in the treatment of lupus erythematosus with carbon dioxid snow. He uses the Pusey technic which he thinks is the best and the easiest. He reports six cases of this dermatosis permanently cured by this procedure.

PARDO-CASTELLO, Havana.

LOCALLY RECURRENT SO-CALLED "FIXE" ERUPTION AFTER ARSPHENAMIN AND MERCURY. E. LEVIN, Dermat. Wehnschr. **72**: 278 (April 9) 1921.

Analogous to the "fixed antipyrine exanthem" is an eruption which may appear after administration of arspenamin or mercury. It may occur after

the first injection or later after the completion of several courses. It may recur with variations, such as the appearance of vesicles, absence of pigmentation and extreme evanescence. No difference has been noted in this respect between the different arsphenamin preparations.

A favorable explanation has not been advanced. Toxic states, nervous influences and exhaustion of the suprarenals predispose. There must be a localized vascular hypersensitiveness. Mercury and novasurol produce similar eruptions.

ANDREWS, New York.

THE INFLUENCE OF HEAVY ROENTGEN RAY AND RADIUM EXPOSURES ON THE GENERATING PROCESS. PAUL WERNER, München. med. Wchnschr. **68**:767, 1921.

A large number of women received roentgen-ray treatment until the cessation of the menses was attained. However, conception was possible, pregnancy and labor took a normal course. A certain disposition to abortion seemed to be developed. Children of mothers who had received roentgen-ray treatment seemed to be impeded in their development. Later on these children seemed to recover from the inflicted damage.

AHLWEDE, Hamburg, Germany.

BLOOD SUGAR ESTIMATION IN PSORIASIS FURUNCULOSIS AND SYPHILIS. W. PICK, Dermat. Wchnschr. **72**:297 (April 16) 1921.

The American authors Schwartz, Heimann and Mahnken, working with the method of Benedict and Lewis, found frequent hyperglycemia in acne, seborrhea and syphilis. Jadassohn and Bloch have called attention to the determination of blood sugar in various dermatoses. The author examined the blood of forty-seven patients for glucose content, using the micro-method of Bang. Two parallel determinations were always made. In fifteen cases of psoriasis there was an almost constant increase in the blood sugar, the average being 135 mg. per hundred cubic centimeters. In seven cases of furunculosis the majority showed a slight increase, and in twelve cases of secondary syphilis six showed a moderate hyperglycemia.

ANDREWS, New York.

CONTRIBUTIONS TO THE PATHOGENESIS OF THE SOFT CHANCER. C. BRUCK, Arch. f. Dermat. u. Syph. **129**, Pt. 2, 1921.

In 1915 Bruck first drew attention to the *Streptobacillus ducrey* of Unna which he found in the vulva and urethra of clinically healthy women. He now publishes a case of a woman infecting her husband with *ulcus molle*. The woman showed no clinical symptoms, although streptobacilli were abundant in the vaginal secretion.

AHLWEDE, Hamburg, Germany.

MERCURY AND GOLD STOMATITIS. J. SCHUMACHER, Dermat. Wchnschr. **72**:305 (April 16) 1921.

Prophylactic extraction of carious teeth is the best preventive of stomatitis in patients receiving extended courses of mercury or gold. Almquist has proved that certain bacteria which grow in carious teeth produce sulphuretted hydrogen which combines chemically with ionized mercury or gold producing a compound which leads to stomatitis. Oxidation of the sulphuretted hydrogen by the use of hydrogen peroxid or potassium permanganate is of therapeutic value

as it prevents the formation of the irritating mercury sulphur compound. Remedies of gold or silver which do not produce mercury or gold ions in the blood and serum, do not cause stomatitis. However, such remedies are not therapeutically effective.

ANDREWS, New York.

MULTIPLE KELOIDS OF THE HANDS AND GRANULOMA ANNU-LARE. E. GALEWSKY, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Undoubtedly keloids of the fingers exist. Though the etiology is unknown, the infectious cause is probable. Old keloids resist treatment unless surgical removal is made. Fresh cases are best treated with the roentgen ray or radium. Granuloma annulare requires immediate energetic internal (arsenic) and roentgen-ray treatment.

AHLWEDE, Hamburg, Germany.

DEVELOPMENT OF CARCINOMA ON PSORIATIC BASIS. A. ALEXANDER, Arch. f. Dermat. u. Syph. **129**: Pt. 1, 1921.

Of the eighteen cases of skin carcinoma developed on psoriasis reported in the literature, eleven must be considered as malignant degeneration of arsenic hyperkeratosis, so-called "arsenic carcinoma." Only seven are most probably genuine psoriasis carcinoma, that is, actual development of psoriatic lesions into carcinoma.

AHLWEDE, Hamburg, Germany.

AN ETIOLOGIC FACTOR IN ANGIONEUROTIC EDEMA: PRELIMINARY REPORT. F. M. TURNBULL, J. A. M. A. **77**:858 (Sept. 10) 1921.

Two patients with angioneurotic edema had an associated chronic sinus infection and diseased tonsils. Radical operation on these foci resulted in cure.

These cases would indicate that there may exist an etiologic factor in these chronic nasal sinus infections which may cast much light on anaphylactic manifestations in general. Certain experimental work along this line is in progress.

MICHAEL, Houston, Texas.

TWO CASES OF PITYRIASIS RUBRA PILARIS. GAERTNER, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

In one of the two cases the father of the patient suffered from pityriasis rubra pilaris from his fifth to his eighty-first year. At the site of the excision of a piece of skin a dense hyperkeratosis was seen to develop (topical exacerbation following trauma as in psoriasis).

AHLWEDE, Hamburg, Germany.

THRUSHMYCOSIS OF THE NAILS IN A CASE OF ARSPHENAMIN. W. FREI, Arch. f. Dermat. u. Syph. **129**: Pt. 1, 1921.

A female patient suffering from arspenamin dermatitis showed saprophytic thrush fungi on the scalp. The fungi were transferred, probably by contact, to the nails where a mycosis developed. Thorough microscopic and serologic investigation in a large number of cases showed that thrush-like fungi seem to be comparatively frequent saprophytes of the skin wherever this is inflamed, macerated or disposes to exudation. Exact investigation is therefore necessary before the etiology of similar conditions is ascribed to these fungi.

AHLWEDE, Hamburg, Germany.

ECZEMA "MIGRANS." A. BLASCHKO, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

The author describes a new form of eczema which has not been mentioned in literature. The condition somewhat resembles eczema seborrhoeicum Unna and some cases of artificial dermatitis. The disorder is designated as "migrans" because it creeps over the body.

AHLWEDE, Hamburg, Germany.

PATHOGENESIS OF THE TRICHOPHYTIDES. B. BLOCH, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

Disorders due to trichophyton fungi form groups which may somewhat correspond to the "tuberculids," that is, *Lichen trichophyticus* corresponds to *Lichen scrophulosorum*; erythema nodosum trichophyticum corresponds to erythema induratum in tuberculosis and syphilis.

AHLWEDE, Hamburg, Germany.

THE NERVOUS ORIGIN OF ANGIECTATIC AND ANEMIC NEVI. A. BUSCHKE, Arch. f. Dermat. u. Syph. **129**: Pt. 2, 1921.

This article reports two cases of widespread nevi anemici Voerner which were combined with angiectatic nevi. Both showed an anomaly of the vasomotory nerves, the primary nerve nevus thus causing the secondary vessel anomaly.

AHLWEDE, Hamburg, Germany.

THE MORPHOLOGY OF SPIROCHAETA PALLIDA STUDIED IN THE DARK FIELD. ANTONI, Arch. f. Dermat. u. Syph. **129**: Pt. 1, 1921.

Attoni observed side branches of *Spirochaeta pallida* on which buds (spores) were developed. In his opinion these buds form new spirochetes. These are, therefore, certainly not protozoan, but vegetative growths akin to the higher fungi.

AHLWEDE, Hamburg, Germany.

NECROSIS OF SKIN FOLLOWING INTRAMUSCULAR INJECTION OF HYDRARGYRUM SUCCINIMID. JADASSOHN, München. med. Wchnschr., No. 27, 1921.

Jadassohn publishes a case of necrosis of the skin following injection of hydrargyrum succinimid from his own observation. He adds this case to the three published by Lesser in 1899 and the case of Bovig who injected red mercuric iodide in oil, published 1901 in the *Annales de dermatologie et syphilographie*.

AHLWEDE, Hamburg, Germany.

ARSPHENAMIN ICTERUS. TACHAU, Deutsch. med. Wchnschr., No. 25, 1921.

Arsphenamin is not the cause of icterus. The expression "arsphenamin icterus" is not correct as in practically all cases following the administration of arsphenamin the icterus is an infectious early syphilitic icterus.

AHLWEDE, Hamburg, Germany.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

DISCLOSURE OF CONFIDENTIAL INFORMATION AS TO CONTAGIOUS DISEASE. J. A. M. A. **75**:1153 (Oct. 23) 1920.

Of interest to syphilographers is a recent decision of the Supreme Court of Nebraska—a court of last resort—on the question of professional secrecy, the case arising out of the disclosure by a physician, as a matter of protection to others, of the fact that one of his patients was syphilitic. *The Journal* thus interprets the decision:

When a physician makes a disclosure, he must be sure that it is necessary to prevent the spread of the disease, and must act in good faith with reasonable grounds for his disclosures and without personal malice toward the infected person. Having observed these precautions, he cannot be held liable, even though he is mistaken in his diagnosis and has stated that his patient is afflicted with a disease that he does not have. In other words, the question at issue is not the accuracy of the physician's diagnosis. The law does not require the physician to be infallible; he is only required to possess the average skill and ability of other physicians in similar circumstances and to exercise due care and skill. Having made a diagnosis to the best of his ability, if he believes honestly and without malice that the patient is a danger to another individual or to the community, he is justified in communicating so much of his belief as may be necessary to protect others from contracting the disease. The decision recognizes the fact that, while the physician owes a duty to his patient, he also owes a duty to his other patients and to the public.

SENEAR, Chicago.

**ABSTRACTORS FOR ARCHIVES OF DERMATOLOGY. AND
SYPHILOLOGY, VOLUME 4, 1921**

C. Guy Lane	Boston
F. E. Senear	Chicago
E. A. Oliver	Chicago
J. Frank Waugh	Chicago
R. C. Jamieson	Detroit
V. Pardo-Castello	Havana, Cuba
E. Ahlswede	Hamburg, Germany
P. D. Gutierrez	Manila, P. I.
J. C. Michael	Houston, Texas
H. R. Foerster	Milwaukee
O. L. Levin	New York
H. J. Parkhurst	Toledo, Ohio
C. M. Williams	New York
G. A. Andrews	New York
L. K. McCafferty	New York
Herman Goodman	New York
C. C. Tomlinson	Omaha
W. H. Guy	Pittsburgh
Frances Spinka	St. Louis

Society Transactions

SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MADRID

Regular Meeting, May 6, 1921

DR. AZÚA Presiding

INTENSE RADIODERMATITIS. Presented by DR. SAINZ DE AJA.

A patient with lupus was treated with radium twenty-four hours with a filter of 2 mm. At first she exhibited the usual radiodermatitis that generally disappears in a couple of months, but in this case it did not happen so, and the dermatitis still remained six months after applying radium, at its maximum intensity, even having become ulcerated.

DISCUSSION

DR. AZÚA said that in spite of all statements there is no way of measuring the action of radium.

DUHRING'S DERMATITIS APPARENTLY CURED BY TURPENTINE.
Presented by DR. AZÚA.

DR. AZÚA tells the story of a patient who for seven years had had successive outbreaks. The lesions healed after being treated with 10 c.c. (2.71 fluidrams) of essence of turpentine, 3 c.c. (48.6 minims) a week, the dose being increased very gradually. Since treatment was begun no rash has appeared, and at present she is free from all lesions. He reports this case as others have already been published. On the other hand, the same procedure has failed in one of Hallopeau's patients who had been treated before with a turpentine preparation and copper compounds intravenously and in whom he did not dare to go beyond a dosage of 15 c.c. (4 fluidrams). The treatment has also failed in a case of pemphigus vulgaris.

DR. COVISA considered interesting the result obtained by Dr. Sainz de Aja with turpentine in Duhring's dermatitis. He stated that he himself had had another case of uncontrollable Duhring's dermatitis cured with calcium chlorid given internally. There may be a recurrence but so far this has not happened.

ARSENICAL ERYTHRODERMA. Presented by DR. SAINZ DE AJA.

DR. SAINZ DE AJA again refers to this patient (presented at a previous session) who has a new arsphenamin erythroderma covered by pigmented points, after receiving the fourth injection. At the suggestion of Dr. Bejarano, the blood was examined and the diagnosis of leukemia excluded. It is especially interesting as it is a fixed exanthem with an arsphenamin melanoderma.

DISCUSSION

DR. AZÚA agreed that silver arsphenamin causes erythemas to such an extent that he considers it an expression of intolerance; arsenical pigmentations, others than erythroderma, are frequent, but their combination with erythroderma is rare.

PARAPSORIASIS IN PATCHES AND HEBRA'S PRURIGO. DR. SAINZ DE AJA.

In both cases Dr. Sainz de Aja has employed pilocarpin as a few cases have been reported cured by this method. The authors, however, disagree greatly as regards dosage since some have given as high as 100 mg. ($1\frac{1}{2}$ grains), which seems incredible. Among patients with parapsoriasis treated by him, only one improved and the other is not yet cured. Twenty milligrams ($\frac{1}{2}$ grain) are being administered now to the latter. In view of the statements as to the curability of parapsoriasis by pilocarpin, Dr. Sainz de Aja wonders whether it is a matter of dosage, and he intends to increase the dosage in one of his patients who is very strong, and watch the outcome. In a case of Hebra's prurigo, he did not have any success with pilocarpin.

DISCUSSION

Dr. Azúa said that he saw a typical parapsoriasis with patches treated by Broca (the patient's father). It was not very serious, but it was stated no cure was possible. The only treatment administered was a fat application and cleaning of the skin. He saw the patient again five years ago, and the condition was the same. In Chicago the patient was treated with pilocarpin, 15 mg. ($\frac{1}{4}$ grain) every other day, a dosage that Dr. Azúa considers dangerous. These patients are not cured, but the condition is not serious. He suggested that turpentine should be tried in these cases.

Dr. Aja said that the important part of the problem is not only the intractability but the intolerance to medication, as even with Lassar's paste the condition of the patients becomes worse as a dermatitis is formed around the patches.

VENEREAL SERPIGINOUS ULCER. Presented by DR. SAINZ DE AJA.

Dr. Aja presented again the two patients exhibited at a previous session. As there were doubts whether the case was granuloma venereum, antimony and potassium tartrate was administered to both of them, 6 c.c. (1.62 fluidrams) a week, every other day. One of them has recovered and the only sign left is a small infiltration on the pubis. In the other case, although the lesion seemed identical, no results have been obtained. In view of the outcome and the clinical appearance, Dr. Sainz de Aja favors a diagnosis of granuloma inguinale if confirmed by the biopsies made by Dr. Arcaute.

CONTINUOUS TREATMENT OF SYPHILIS. Presented by DR. SAINZ DE AJA.

Dr. Sainz de Aja considers it wise to take up the question of the continuous treatment of syphilis. In his opinion treatment should be continuous. Nowadays we have means to do so, as there are available two different classes of drugs. In order to prevent the serologic aggravations observed at present, he believes the courses should be alternated instead of alternating the injections of mercury and arsenic.

DISCUSSION

Dr. Covisa stated that at first he was against continued medication as he thought it might produce toxic effects. However, as soon as medication is suspended with the present neo-arsphenamin new lesions appear. The only solution, therefore, is to apply a continual medication although one would rather resort to this measure only in rebellious cases.

Dr. CRIADO had intended to bring up the questions as to when treatment should be stopped, when may syphilis be considered cured and when marriage may be authorized. He thinks some conclusions should be established which should represent not one person's opinion but the whole society's.

Dr. BARRIO DE MEDINA, Secretary.

MINNESOTA DERMATOLOGICAL SOCIETY

Aug. 5, 1921

C. D. FREEMAN, M.D., *President*

DERMATITIS HERPETIFORMIS. Presented by Dr. SWEITZER.

Mrs. S., a middle-aged woman, had suffered from Duhring's disease for the last eighteen years. Considerable improvement had resulted recently under treatment with ultraviolet rays.

DERMATITIS HERPETIFORMIS. Presented by Dr. MICHELSON.

A man, aged 70, showed an extensive eruption, with grouping, of papules, vesicles and bullae on the body, face and scalp. The disease first appeared thirty years ago. The eruption had been a source of considerable annoyance to the patient, but had not affected his general health. The eruption was responding favorably to arsenic.

DERMATITIS HERPETIFORMIS. Presented by Dr. SWEITZER.

A young man, aged 20, at the time of presentation had only a few lesions, as he had shown great improvement after exposures to ultraviolet rays. The eruption had been extensive and had started three years ago.

DERMATITIS HERPETIFORMIS. Presented by Dr. BUTLER.

A man, aged 35, in whom the disease had existed for eight years, presented the grouped eruption on the lower extremities and on the left shoulder. He had obtained relief from the burning and itching after weekly exposures to ultraviolet rays.

DERMATITIS HERPETIFORMIS. Presented by Dr. OLSON.

Two years ago, the patient, a lawyer, aged 33, had influenza and was given an injection of horse serum to control a hemorrhage. Following the injection of horse serum, there appeared an extensive eruption of giant urticaria. As this giant urticaria subsided, there were noted the papular and vesicular lesions of Duhring's disease. One attack had been bullous in character. At the time of presentation, the lesions involved the body, arms, legs and scalp. There had been little response to autoserum, ultraviolet light, etc. He had been very nervous, but with rest and life outdoors, with no other treatment, had improved in general health.

A man, aged 38, was in good general health in spite of a skin eruption of many years' duration. He was a blond, with blue eyes and flaxen hair. Owing either to Duhring's disease or the arsenic which he had taken some years ago,

the skin had become intensely pigmented, and the patient appeared swarthy. He had obtained most relief from a 5 per cent. liquor carbonis detergens shake mixture.

DISCUSSION

DR. BUTLER stated that many patients had been treated with ultraviolet rays with favorable results. He had used the lamp on one patient and the lesions had cleared up remarkably well, but had recently recurred.

DR. O'LEARY said that they had recently treated two patients with ultraviolet rays with relief for a short time only, the symptoms soon returning with even greater severity.

DR. GOECKERMANN thought that they had obtained the greatest and the quickest relief from the use of the roentgen ray. Recently, he had given two one-fourth skin units with immediate relief from itching.

DR. IRVINE stated that at times the roentgen ray gave good results, but that at other times no benefit was seen.

DR. QUINN said that he had used the roentgen ray on a patient recently with good results, the patient being benefited more by the use of the roentgen ray than by any other line of treatment.

DR. FOERSTER called attention to the value of autogenous serum.

DR. CREGOR spoke in favor of the roentgen ray, but he had also found sulphur and salicylic ointment of great value.

DR. MITCHELL said that in their experience the roentgen ray was of great value when there was marked grouping of the lesions. Autogenous serum was a valuable measure.

DR. WAKEFIELD stated that he was interested in seeing so many patients with Duhring's disease at one time. In his experience, patients obtained benefit from sulphur baths and a dusting powder containing 10 per cent. sulphur.

PEMPHIGUS VULGARIS. Presented by DR. MICHELSON.

A woman, aged 36, born in Norway, had lived for the last eight years in this country. Last March she was suddenly taken ill with a chill and high fever. A flaccid bullous eruption had appeared in the mouth and over the entire body. At intervals, she had had fever, followed by a fresh outbreak of bullae. Her physical condition was good and she had not lost much strength. All physical and chemical tests were negative. Phototherapy had greatly relieved her condition.

PEMPHIGUS VULGARIS. Presented by DR. KLEIN.

A woman, aged 30, showed a moderate grade of pemphigus of eighteen months' duration. The lesions first appeared in the mouth.

EPIDERMOLYSIS BULLOSA: TWO CASES. Presented by DR. OLSON.

A sister and a brother, aged 9 and 13 years, respectively, had suffered from large bullae since birth. The father and an uncle were affected with the same trouble. The bullae in most of the attacks were large, some as large as a hen's egg, and were limited to the feet. The bullae appeared only during the summer. At the time of presentation, the bullae were few in number and small. Thorough search for the epidermophyton had been negative. The patients had been under observation for two years, and clinically the condition appeared to be epidermolysis bullosa, limited to the feet.

DISCUSSION

DR. KESSLER stated that the children were more liable to bruise their feet in the summer, and thus produce the bullae.

DR. OLSON stated that the children had been under observation for two years, during which careful examination for the epidermophyton had been negative. Treatment with Whitfield's ointment had given little or no benefit.

DR. IRVINE said that he had seen the patients over an extended period and agreed with the diagnosis of epidermolysis bullosa.

CASE FOR DIAGNOSIS: POSSIBLE SPOROTRICHOSIS. Presented by DR. IRVINE.

A man, of middle age, from the state prison, was shown with numerous ulcers and abscesses, located especially about the elbow joints. The patient had been treated with the iodids and copper. The condition had first appeared following an injury to the hand, a splinter of wood having entered the palm.

DISCUSSION

DR. SUTTON said that they had had thirty-seven patients with sporotrichosis. The majority of the cases had followed some injury, such as the peck of a chicken or the bite of a dog. Diagnosis in this patient was impossible without a culture.

DR. QUINN thought the patient was suffering from tuberculosis. There were discharging sinuses leading down to the bone.

DR. CREGOR doubted that the patient had sporotrichosis.

DR. LAIN stated that he did not know whether sporotrichosis was more common in the South, but he saw eight to ten cases a year. The cases clearly follow the lymph nodes.

DR. FOERSTER called attention to the bone and pulmonary types of sporotrichosis, especially described by the French, which give an entirely different clinical picture from the ordinary superficial sporotrichosis.

PAPULONECROTIC TUBERCULID; TUBERCULOUS ADENITIS; SCROFULODERMA; SCROFULOUS GUMMAS. Presented by DR. MICHELSON.

A man, aged 30, born in Norway, had lived in the United States for the last sixteen years. His skin eruption developed eight years ago, and since then the skin had never been normal. Two years ago, a gland was removed from the neck, and left a discharging sinus. The eruption consisted of pink to red superficial papulopustules, situated on the forearms, abdomen and face. On the legs, the lesions were larger, but had the same general characteristics, with deeper ulceration. Biopsy of one of the lesions of the skin revealed typical tuberculous structure, with numerous giant cells.

HEALED FOLLICLIS; ACTIVE LUPUS ERYTHEMATOSUS. Presented by DR. MICHELSON.

Mrs. S., aged 35, had had a recurring eruption on the skin since she was 11 years old. At that time, the eruption was on the hands, arms and legs, and healed with the characteristic scars of folliclis. The eruption had recurred

for many years. Eleven years ago, lupus erythematosus appeared. At the time of presentation, the patient showed the scars of folliculitis, and active lupus erythematosus on the face and scalp.

TROMBIDIOSIS. Presented by DR. MICHELSON.

A Greek, aged 31, a railway laborer, had been employed cutting weeds. For a week before presentation, he had suffered agonies from a widely scattered, intensely itching eruption, due to the bites of the red jigger. The eruption had first appeared on the legs and genitals, and later over the body. The eruption consisted of a dark red wheal, with a central puncta. The newer lesions were pink in color. The lesions varied in size from a nickel to a dollar. The itching was intense, constant, and not relieved by treatment.

DISCUSSION

DR. McEWEN inquired as to the distribution of the jigger.

DR. OLSON stated that the red jiggers or *Trombidium irritans* are widely distributed over the United States. They are especially prevalent on the bushes, vines and grass near the shores of lakes. They are extremely common about the lakes in Minnesota. The best treatment is removal with a needle, which is fairly easy shortly after infestation, before the jigger has had time to burrow into the skin or hair follicle.

DR. LAIN said that jiggers are very common in Oklahoma. This year they were particularly abundant. Some climatic conditions, such as rain, seems greatly to affect the number of these mites.

THRUSH. Presented by DR. OLSON.

Florence R., aged 7, had suffered from thrush for the last two and one-half years. The disease involved the mouth and probably the esophagus. In the mouth, white patches could be seen, extending back from the commissures, and on the tongue, especially along the sides. The white pellicle that formed showed the thrush fungus—*Oidium albicans*. Diagnosis had been further confirmed by culture. The disease had existed for two and one-half years and had resisted all treatment, such as glycerite of boroglycerin, silver nitrate, copper sulphate and potassium iodid. The general health had been good. Since shortly after birth the patient had, at intervals, impetiginous and echthymatous lesions on various parts of the body. Part of the left eyelid and part of the nasal cartilage had been destroyed by these abscesses.

URTICARIA PIGMENTOSA IN THE ADULT. Presented by DR. OLSON.

Mrs. G., aged 36, presented a yellowish-red papular eruption on the arms, legs and body. It first appeared eight years ago. On rubbing, the lesions became more pronounced. There had been no itching. The papules had remained practically unchanged for the past eight years. The condition resembled a papular syphilid and xanthoma. The Wassermann reaction was negative and the urine free from sugar. Biopsy revealed the presence of urticaria pigmentosa, with large numbers of mast cells.

SYPHILITIC DACTYLITIS. Presented by DR. OLSON.

Kenneth L., aged 4, an orphan, was first seen about a year ago. At the time there was a large swelling of the right and left little fingers. The patient was mentally deficient, unable to talk at all, and very stubborn. His Wassermann reaction was positive. Following antisyphilitic treatment, there was a rapid and pronounced improvement in the mental condition, and he was able to say some words. The swelling of the fingers decreased. Some weeks after beginning treatment, there was a discharge from both little fingers. These discharging sinuses had gradually healed.

BROMODERMA TUBEROSUM. Presented by DR. OLSON.

Mrs. W., aged 31, had been treated with bromids for some obscure nervous trouble. In June, 1921, there was a mild acne-like eruption of bromoderma, which soon disappeared. In July, 1921, there appeared an irregularly round vegetating lesion, about 3 inches (7.6 cm.) in diameter on the right shin. There was considerable inflammatory reaction, accompanied by pain. Many miliary abscesses were noted. The condition gradually improved under ointment of ammoniated mercury.

MORPHEA. Presented by DR. KLEIN.

A young woman noted, last August, a red blotch on her forearm, which later became purple. The physician whom she consulted made a diagnosis of ringworm, and applied tincture of iodine. During the winter the lesion became lighter, which was thought to be a sign of improvement. At the time of presentation, there was a distinct, sharply defined ivory-colored area, which was indurated and surrounded by a purplish halo. At times there had been itching.

NEUROTIC EXCORIATION. Presented by DR. MICHELSON.

A man, aged 62, for the last ten years had suffered from an irresistible desire to dig at the scalp with the nails. There had been a crawling sensation which was not relieved until the skin was broken. This was usually done at night, the patient digging at a different spot each evening. There was no attempt at deceit. He frankly admitted the act, but said he could not refrain from so doing. He had a perforated septum and a positive Wassermann reaction. His general condition responded to antisyphilitic therapy, but the excoriations were not altered. Advice concerning his condition had helped him in controlling the desire to dig into the scalp.

ELEPHANTIASIS. Presented by DR. MICHELSON.

Mrs. J., an American, for the last seven years had been troubled with a gradual enlargement of the left leg. During this period, she had had attacks which were characterized by very high fever, lasting for about forty-eight hours, when the temperature would return to normal, and she would not be troubled for a period again. The leg was enlarged to about twice its normal circumference, and was decidedly warty and purplish. The itching was intense and there was a certain amount of local pain. The patient had never been in the tropics, but at one time had had a boarder who had spent much time in the tropics. He, however, was not troubled with the disease.

The patient refused biopsy. During her stay in the hospital she had an attack. The temperature reached 104.5 F., and she had a very severe chill. Search for the filaria on various occasions, both day and night, were unfruitful.

LICHEN PLANUS ERYTHEMATOSUS. Presented by DR. CRUME.

Mr. S., aged 35, had noticed an eruption on the front of the forearms, near the wrists and extending upward, for the past three years. There were no subjective symptoms, such as itching. The color was violaceous, and there was, apparently, a slight atrophy with the healing of the lesions. No typical lichen planus papule had been noted. Biopsy revealed the rather characteristic infiltration of round cells, sharply defined below. The changes in the epidermis corresponded to those of lichen planus.

SARCOMA OF KAPOSÍ. Presented by DR. MICHELSON.

The lesions in this patient, a middle aged man, of Scandinavian origin, were present on the feet and legs.

EPITHELIOMA: RESPONSE TO RADIUM AFTER FAILURE TO RESPOND TO ROENTGEN RAYS. Presented by DR. OLSON.

A man, aged 53, had had an epithelioma on the right cheek for the last seven years. For eighteen months, recently, he had been treated at intervals of six weeks, with sixteen apparently large doses of roentgen ray. There was some improvement, but not sufficient to prevent further growth. A half strength radium plaque, unscreened, was applied for four hours, June 13, 1921, with complete disappearance of the tumor.

LEPROSY. Presented by DR. IRVINE.

A man, aged 62, born in Norway, had lived in the United States for the last thirty-one years. Seven years ago, he noticed a peculiar eruption on the face and hands, which had gradually become worse. His general health had been good. The patient showed a nodular, infiltrated, brown-red eruption on the face, forehead and hands. There was marked leontiasis. The ulnar nerve was thickened and rope-like. Leprosy bacilli were found in the nasal secretion and by biopsy.

LEPROSY. Presented by DR. IRVINE.

Mrs. W., a young woman, born in Minnesota, showed the beginning eruption of leprosy. Diagnosis had been confirmed by the finding of lepra bacilli.

PRURIGO. HODGKIN'S DISEASE. Presented by DR. MICHELSON.

Mrs. V., aged 31, had one child four years ago, who is living and well. One year ago, her feet and hands began to itch. She applied to a physician for relief, and was given sulphur ointment. The itching continued, and seemed to spread over the body. She went to another physician, who ordered mercury rubs. About that time, the glands in the neck and axillae began to enlarge. The itching over the body became more intense. The patient would scratch the lesions until bleeding occurred. One of the small glands in the neck was removed and examination revealed the presence of Hodgkin's disease. The roentgen ray and radium had caused a considerable diminution in size of the enlarged glands. At the time of presentation, the surface of the body showed

numerous linear scratch marks, and a high degree of lichenification. The itching had been intense and resistant to treatment.

KERATODERMA BLENORRHAGICA. Presented by DR. GAGER.

A man, aged 41, single, a glazier by trade, had had his first attack of gonorrhea at the age of 21. This had cleared up rapidly, but, at 27, he had a urethral stricture and acute retention. Treatment gave permanent relief. July 2, 1921, he noticed a purulent discharge from the urethra. July 5, he developed a balanitis. July 9, he noticed an eruption on the arms and legs. The skin lesions began as a vesicle on an erythematous base. The vesicles soon became pustular and hyperkeratinized. The base was raised and covered with thick scales. Some of the larger lesions had several layers of scales and were conical in form. The eruption was somewhat grouped, but scattered lesions were found on all parts of the body. There were groups of lesions on the buttocks, thighs, legs, feet, arms and forearms. The most characteristic lesions were seen on the feet. The Wassermann reaction was negative. Sinears from the urethra and the skin lesions showed numerous pus cells, and an extracellular, gram-negative diplococcus.

DISCUSSION

The members and visitors all agreed with the diagnosis and called attention to the extreme rarity of true cases of gonorrheal eruptions of the skin.

ARSPHENAMIN DERMATITIS. Presented by DR. GAGER.

Mrs. C., aged 30, had applied, Dec. 8, 1920, for treatment for a generalized rash and other typical signs of secondary syphilis. She was given six doses of 0.6 gm. neo-arsphenamin, at weekly intervals. In March, 1921, she was placed on mercury inunctions. In May she was given eight doses of 0.6 gm. (9.26 grains) neo-arsphenamin. At the time she complained of dizziness. The Wassermann reaction of the spinal fluid was positive, the cells were 33 per cubic millimeter, and the colloidal gold test was negative. July 9, she developed an acute dermatitis of the face and neck. The skin about the eyelids was swollen and thickened. There were numerous keratoses on the hands, irregular in outline and yellowish.

MINNESOTA DERMATOLOGICAL SOCIETY

Aug. 6, 1921

Cases Presented by DRs. STOKES, O'LEARY and GOECKERMANN
from the Mayo Clinic

SARCOID WITH VISCERAL LESIONS.

A young woman, aged 29, showed lesions on the nose, the left cheek and the arms. The condition started some years ago. Roentgen-ray examination showed pulmonary fibrosis, and there was some involvement of the lymph nodes. The Wassermann reaction was negative and there was no response to arsphenamin. The blood picture was normal.

DISCUSSION

DR. MITCHELL was not optimistic as regards the cure of this condition. They had used various methods of treatment, including arsphenamin therapy. One patient made a marked improvement under arsphenamin, but later reported in a condition worse than that existing when treatment was started.

DR. SWEITZER also called attention to the difficulty of effecting a cure, but suggested freezing with carbon dioxid snow for the lesions on the face.

CASE FOR DIAGNOSIS.

A man, aged 34, presented a large ulcerating lesion on the left arm, associated with necrosis of the bone. The condition began in 1908, as a subcutaneous nodule on the forearm, and extended peripherally. The distribution of the lesions was somewhat suggestive of sporotrichosis. The sporothrix had not been found, and biopsy showed no evidence of epithelioma. There had been no response to potassium iodid, roentgen ray or antisypilitic treatment. There was slight improvement under intravenous injections of tartar emetic.

DISCUSSION

DR. MITCHELL suggested the possibility of dermatitis factitia.

DR. STOKES stated that the patient had been in the hospital with a severe hemorrhage following a perforating abscess of the axilla. The hemoglobin was reduced to 30 per cent., and he was so weak he could hardly move. During the time that he was in the hospital, the lesions were bandaged at all times, and he was under the care of two nurses.

DR. BUTLER said the condition impressed him as one of prickle cell epithelioma.

DR. McEWEN suggested cancer as a diagnosis.

DR. IRVINE called attention to the resemblance to granuloma inguinale in resisting all forms of treatment.

PEMPHIGUS FOLIACEUS.

A young woman, aged 20, had lesions, including bullae, involving the entire body. The mouth and genitals were not involved. The condition had been present for two years. She showed great improvement under tartar emetic. Cultures from the bullae were negative.

DISCUSSION

DR. SUTTON believed that an autogenous vaccine would be of value.

LUPUS VULGARIS.

A man, aged 32, had extensive patches of lupus on the forehead, right cheek, left arm, back and chest, which started in 1906, at which time the patient had been vaccinated. He had been treated with acid solution of mercuric nitrate and roentgen rays with fair results.

DISCUSSION

DR. SWEITZER advised excision of the area on the arm and thorax.

LUPUS VULGARIS WITH RAPID GLANDULAR INVOLVEMENT.

A man, aged 39, had had a small lesion on the forearm, showing a few apple jelly nodules, and marked lymphangitis, with glandular enlargement in

the axilla. The disease began one year ago. There was no evidence of tuberculosis elsewhere. The case was shown as an unusual type of cutaneous tuberculosis, with an inconspicuous primary focus, and rapid and extensive involvement of the lymph glands. Chicken inoculations had been negative.

ERYTHEMA INDURATUM.

The patient, a woman, aged 44, had had many ulcerative lesions, which healed rapidly under injections of arsphenamin. At the time of presentation, the patient showed a recurrence, which she stated was 50 per cent. less severe than the previous attack. She had been free from symptoms for two years, following six injections of arsphenamin.

DISCUSSION

DR. BUTLER doubted the value of arsphenamin in erythema induratum. He stated that most of the benefit came from the hospitalization of these patients, with complete rest in bed.

DR. STOKES stated that their patients were not hospitalized: they went about their occupation as usual.

REINFECTION OR RECURRENCE OF CHANCER.

In March, 1918, the patient, a young man, had a typical primary lesion on the penis. After two arsphenamin injections, he had been called into the navy, and no further treatment had been given. He remained free from symptoms. In January, 1919, the blood and spinal fluid were negative. A short time before presentation the patient had a number of lesions on the penis, resembling herpes. Spirochete examination was negative, and the Wassermann reaction, taken at a three-day interval, had been ++ and +++.

DISCUSSION

DR. MITCHELL stated that true reinfections were extremely rare, and that he had never seen an undoubted case of reinfection of syphilis.

GRANULOMA INGUINALE.

A man, aged 32, had had, for three years, typical lesions of granuloma inguinale. At the time of presentation, there was an ulcerating lesion involving the groin, pubes, perineum and buttocks. He had had thorough treatment for syphilis. Good results had been obtained with tartar emetic intravenously, but it had been necessary to discontinue treatment because an eighth nerve deafness had occurred. The patient had received from 5 to 10 c.c. (1.35 to 2.71 fluidrams) of a 1 per cent. potassium and antimony tartrate, sterilized by Berkefeld filtration.

CHRONIC IDIOPATHIC ATROPHY.

A young man, aged 22, was presented with patches of atrophy involving different parts of the body. The disease began eleven years ago.

DR. FOERSTER agreed with the diagnosis.

DR. IRVINE stated that he had never seen a case in which the disease started so early in life.

PEMPHIGUS.

A woman, aged 52, showed lesions in the mouth, with definite bullae in the pharynx and larynx. There were no lesions in the skin.

DISCUSSION

DR. STOKES stated that they had seen six similar cases, in which the skin and genital lesions appeared later, with a fatal issue in from three to six months.

DR. FREEMAN inquired as to the possibility of Vincent's disease.

DR. GOECKERMANN said that Vincent's organisms were absent.

DR. BUTLER called attention to the resemblance to trench mouth.

DR. FOERSTER stated that last year he saw a patient who had a typical Vincent's disease. Later the patient returned with lesions of pemphigus.

DR. STOKES stated that Vincent's organisms were found in carcinoma of the tongue, etc., so that the finding of these organisms did not necessarily have much significance.

LUPUS ERYTHEMATOSUS DISSEMINATUS.

A man, aged 48, complained of erythematous patches on the face, neck, fingers and palms. There was definite evidence of atrophy. He had a marked alopecia, and lesions in the mouth which were not definitely bullous in character. The patient was rather lethargic. There was no history of diarrhea.

DISCUSSION

DR. CREGÓR made a diagnosis of pellagra.

DR. WAKEFIELD agreed with the diagnosis of pellagra.

URTICARIAL DERMATITIS WITH PIGMENTATION FOLLOWING THE INJECTION OF ARSPHENAMIN.

A man, aged 35, showed a plaque of urticarial dermatitis, the size of a quarter, above the right wrist. There was moderate pigmentation. This lesion had followed an arsphenamin injection. Further injections of arsphenamin had always been succeeded by a recurrence of the rash in exactly the same place. The patient had used a phenolphthalein laxative, but tests for this drug were negative. Skin tests for arsphenamin had not been made.

FOLLICULITIS.

A blacksmith, aged 36, showed a folliculitis involving the beard, scalp, chest, abdomen and thighs. The eruption had recurred every summer, regardless of the kind of work he engaged in.

DISCUSSION

DR. LANE believed the condition to be due to sodium borate, which the patient used in welding. The freedom from perspiration explained the lack of symptoms in winter.

RECURRENT HERPES.

A young woman had had recurring attacks of herpes on the face for several years. No focal infections were found and there was no evidence of syphilis.

DISCUSSION

DR. CREGOR advised the use of the galvanic current.

DR. MITCHELL stated that they had used the roentgen ray in herpes of the menstrual type, and herpes genitalis in men, with great success.

DR. LANE said that for many years he had recommended the galvanic or high frequency current in the treatment of herpes.

DR. FOERSTER mentioned a case of herpes on the cheek, which followed the use of unskimmed bouillon.

THROMBO-ANGITIS OBLITERANS.

The patient, a young man, not Jewish, showed ulceration of the left foot and marked circulatory disturbances in both feet. He smoked a large number of cigarets. Ringer's solution had been given with little result. The blood sugar was increased.

MYCOSIS FUNGOIDES.

A man, aged 71, showed ulcerating lesions and other lesions of mycosis fungoides of six years' duration. Foreign protein had been tried for the relief of the itching, but no improvement had resulted.

WENDE'S NODULAR TUBERCULOSIS OF THE HYPODERM, SHOWING BENEFICIAL EFFECTS OF ARSPHENAMIN.

A woman, aged 27, showed several nodules on the thighs and lumbar region. The condition had been present for six years.

OLSON, Secretary.

PITTSBURGH DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Sept. 29, 1921

J. G. BURKE, M.D., *Presiding*

PEMPHIGUS CHRONICUS. Presented by DR. CRAWFORD.

A woman, aged 64, one year ago, developed a simple conjunctivitis, which was followed a few weeks later by small bullae on the alae of the nose and one of the pharyngeal mucosa. Deglutition was painful. This state continued for one year, marked by remissions and recurrences, when a few months ago, during an attack of grip an eruption of bullae with clear contents, varying in diameter from 3 to 15 mm., occurred on the chest, axillae and inner thighs. This eruption subsided after five weeks. About one month ago, a fresh outbreak occurred in the left axillary region. Since the beginning, over one year ago, small bullae have appeared on the conjunctiva, anterior nasal and pharyngeal mucosae, as well as on the cutaneous surface of the eyelids. The patient had noticed increasing fatigue.

DISCUSSION

DR. JACOBS asked whether in the opinion of the presenter the form of arsenic used in these cases had any bearing on therapeutic results; he had seen sodium cacodylate effective when other preparations failed.

DR. CRAWFORD said that he felt that the cacodylate was probably the least effective of the arsenicals.

LUPUS ERYTHEMATOSUS. Presented by DR. BURKE.

A girl, aged 17, who gave a history of rheumatism, one year ago noticed red areas in back of both ears and a spot under the left eye which gradually healed. Four months ago she noticed that these areas became red and new spots appeared on the cheeks, forehead and scalp. When first seen two weeks prior to presentation she showed numerous dime to quarter size red, elevated, slightly scaly areas on the nose, forehead, cheek, scalp and back of the ears. Some of the spots were atrophic with patulous follicular openings. A diagnosis of lupus erythematosus was made and with the history of arthritis it was felt that the same etiologic factor might be responsible for her eruption. Under a mild soothing ointment the eruption had improved rapidly for two or three weeks prior to presentation. The patient stated that the atrophic areas had appeared one year ago and the spots of four months' duration were those that at the time of presentation showed as erythematous areas. The diagnosis of lupus erythematosus was offered for the older lesions. The diagnosis was left open on the latter lesions because of the change that had taken place in them in two weeks time. Erythema multiformi or some toxic eruption might be considered. Her Wassermann reaction was negative and no internal treatment had been given.

DISCUSSION

DR. CRAWFORD stated that this was one of a group of patients with unusual cases who endured treatment very poorly. He agreed with the diagnosis.

DR. WERTHEIMER felt that the lesions behind the ears were those of lupus erythematosus and that in his mind such a diagnosis might well be accepted for the entire condition.

DR. GUY stated that he agreed with the diagnosis of lupus erythematosus of the atrophic lesions, and while he was not prepared to dispute the diagnosis of lupus erythematosus of the scalp eruption, he felt that an alternate diagnosis of seborrheic dermatitis should be considered.

DR. HOLLANDER stated that the scalp eruption to him was strongly suggestive of seborrheic dermatitis.

FACTITIOUS DERMATITIS. Presented by DRs. GUY and JACOB.

A girl aged 20, had an irregularly oval ulcer of nine years' duration located in the lower right abdominal quadrant. The case had been under observation three months and the ulcer had improved and relapsed twice in that time. The lesion first developed following an appendectomy a little over nine years before. The ulcer had been excised and cauterized ten or twelve times, only to recur promptly. Notable in the ulcer was the absolute lack of healthy granulations, its necrotic base and extreme chronicity. At the time of the most recent exacerbations a linear brown mark was noted running down the thigh from the wound for a distance of about 3 inches. (This mark has since disappeared by exfoliation.) A biopsy revealed only the presence of an ischemic ulcer with considerable necrosis. Her Wassermann reaction and a therapeutic test were negative. Bacteriologic examination of scrapings from the wound revealed the presence of a mixed infection of no particular significance. Blood examination revealed a mild secondary anemia which is not surprising when one learns that she had been practically bedridden nine years.

DISCUSSION

DR. CRAWFORD stated that he agreed with the diagnosis.

DR. GUY stated that in support of the clinical diagnosis was the report of a neurologist that the girl was of a definite hysterical type. One noted with interest the fact that the ulceration improved as long as a certain nurse was in attendance and that when she was relieved from duty the ulceration extended. An underlying basis of sexual inversion might be the explanation.

CASE FOR DIAGNOSIS. Presented by DR. CRAWFORD.

A man, aged 20, an electric welder, 2 inches below the gluteal fold on the inner, upper, left thigh had an elongated skin affection of one year's duration. The lesion was 9 cm. long and 1.5 cm. in width, pinkish, and cicatricial in appearance, and to palpation was quite hard, somewhat suggesting keloid. The center showed an ulceration about 2.5 cm. in diameter with a slightly elevated purplish-red serrated edge, the surface being of slight capillary appearance. The patient had received eight injections of arsphenamin during the past year with no benefit. He also presented an acro-asphyxia.

DISCUSSION

DR. SCHWARTZ stated that he was very much interested in the ulcer case because he had had the pleasure of seeing the man a few weeks after the ulcer developed. He recalled very accurately that the clinical appearance of the ulcer at that time was that of syphilis and that he had received some anti-syphilitic treatment but did not improve.

DR. CRAWFORD said that a biopsy of this case was made and that the section showed a great number of plasma cells, perigranular and perivascular, so that appearance was that of a granuloma. The plasma cell infiltration was evident in this case, but a definite diagnosis could not be made.

VON RECKLINGHAUSEN'S DISEASE. Presented by DR. HOLLANDER.

Miss C. R., an American woman, aged 32, from the University Dispensary, gave the following history. About two years before presentation several small painless noninflammatory, sessile lumps and areas of pigmentation appeared, scattered over the entire body. The disease had been progressive. Twelve years ago a growth together with the left eye was removed and proved to be sarcoma. Biopsy showed the present tumors to be neurofibromas.

FAVUS. Presented by DR. WERTHEIMER.

A young man, aged 22, had over the entire scalp, many pea-sized, sulphur-yellow cup shaped crusts pierced by hairs. Removal of the crusts showed superficial ulcerations. Atrophic scars were present, and there were areas of complete alopecia. The condition started when the patient was 4 years old. His mother, English born, was first affected, then the patient, the oldest, and each succeeding child.

SYCOSIS. Presented by DR. BURKE.

A man, aged about 50 years, a street cleaner, was presented to show the good result obtained by nonepilating doses of roentgen rays. Former attacks had been cured by roentgen-ray epilation. The presenter called attention to the presence of a resistant chronic conjunctivitis as a likely source of reinfection. He felt that in a case of this sort roentgen rays should be used with caution.

NEVUS LIPOMATODES. Presented by DR. CRAWFORD.

A young man, aged 22, had a congenital asymmetrical nevus of a soft, flabby, fatty nature, elevated from 2 to 8 mm. above the skin surface, of a pinkish-yellow color. The surface presented many rounded papillomatous formations. The nevus extended from the left temporal region downward posteriorly to the ear, fusing with an area extending from the left cheek and coursing downward over the left neck, the entire left pectoral region and left shoulder. At the left shoulder were tumors suggestive of fibroma pendulum. Beneath the chin was a large diffuse fatty tumor formation with normal skin covering. The rest of the body surface presented sac-like projections and islands of pigmentation of von Recklinghausen's disease.

BENIGN SARCOID OF BOECK (LARGE NODULAR TYPE). Presented by DR. CRAWFORD.

A young woman, aged 24, eight years ago developed small plaque-like infiltrations at the left malar region and beneath the left ramus of the lower jaw. During this period the condition was slowly progressive, occasionally marked by a remission, never entirely disappearing. At the time of presentation the area at the left malar region was an oblong infiltrated plaque, 3 by 6 cm., slightly elevated, with a smooth surface, a livid pink, sharply margined, and on close examination presented a fine capillary network. Under the diascopie there was an appearance "suggestive of sand." The patient had no subjective symptoms except an occasional itching sensation. There was a larger plaque of similar description, square in shape, about 6 by 6 cm., and involving the skin over the left lower ramus. On the right forearm there had been a similar plaque (patient's own statement) of four years' duration, which had disappeared during the last year. On the left forearm, anterior surface, there was a small dime-sized area of lichen scrofulosorum.

KELOID. Presented by DR. WERTHEIMER.

A girl, aged 18, following an eruption of "little boils" one year ago developed over the sternum, right side of the neck and arms, pea to cherry sized, red, smooth, shining, firm nodules, oval, linear round in contour. On the right side of face was a pea sized red nodule with central pustulation. About twenty lesions in all were present.

DISCUSSION

DR. CRAWFORD stated that it was a very unusual type of keloid and that it belonged to the infectious type of keloids.

DR. WERTHEIMER said that in his opinion the case was one of keloid following follicular infection in a patient predisposed to the development of keloid very much the same as in the negro skin.

SARCOMATOSIS. Presented by DRs. GUY and JACOB.

A man, aged 40, a laborer, stated that a year before presentation his left foot had been injured. When presented he had a purplish tumor located between the left great toe and the one next to it and a marked involvement of the neighboring glands. There were also present numerous pigmentary lesions scattered over the face. When he was first seen by the presenter, about three months ago, the primary lesions were definitely hemorrhagic in

type. Since that time the condition has been progressive, and he has developed considerable cachexia. As a palliative treatment, radium was applied to the primary growth locally with considerable improvement.

DISCUSSION

DR. RAY stated that he had examined specimens from the primary growth and from the neighboring glands. There was no difficulty in making a diagnosis of sarcoma, but the presence of different types of cells made a definite pathologic classification of the type of sarcoma somewhat difficult.

Book Reviews

DISEASES OF THE SKIN. By J. M. H. MACLEOD, Physician for Diseases of the Skin, Charing Cross Hospital. Pp. 1307, with 23 illustrations in color and 435 figures in black and white. New York: Paul B. Hoeber, 1921.

Since the publication of Crocker's fine book on diseases of the skin, the British school of dermatology has been giving us abridged textbooks on diseases of the skin. We have had the excellent smaller books of Morris, Walker, Whitfield, Sequiera, and others. But the comprehensive books have been American. MacLeod now comes to us with a treatise, like some of the recent American works, in which as little concession to space is given as is practically possible. He gives the British a work which is the natural successor to Crocker's.

This work by MacLeod rouses great expectations, and must meet exacting requirements. It cannot but bear comparison with Crocker's book, which was generally regarded as one of the great books on dermatology. MacLeod, too, occupies a position of great respect among dermatologists. His book on the pathology of the skin has been a handbook for dermatologists for nearly twenty years and has won for him their gratitude. His various other contributions to dermatology have been of the same respect-commanding sort. It is natural, therefore, that his *opus magnum* should be received eagerly.

It may be said, in general, that the book is a good one. It covers dermatology with proper emphasis on the proper subjects, and with due consideration for the space which should be given to them. It is in nowise an imitation of Crocker, but it strongly resembles in its characteristics Crocker's book. It has the same sound British clinical judgment. It is based on an enormous experience, and it has the background of an accurate knowledge of cutaneous pathology; so it may be regarded as the mature expression of a man whose training is so thorough and whose experience is so great in his field, as to entitle all of his views to respect. It is, then, a real addition to the textbooks on dermatology.

The book, however, has a good many minor defects. It contains in the section on treatment many uncritical statements; for example, the proprietary "Collosool Manganese" (which has been refused recognition by the Council on Pharmacy and Chemistry), as well as tin oxid, and calcium sulphid are cited as used in the treatment of boils without any critical estimation of their value or lack of value. The author's style is careless: "Iodine and the iodides have an alterative effect on the skin, causing . . . absorption of certain gummatous lesions." He means, of course, that they have an alterative effect on tissues, not particularly the skin—whatever "alterative effect" is. His English is careless. He has, for example, a fondness for the use of subjunctive verbs in conditional sentences under any circumstances. In one paragraph, he uses "if it be" and "if there is" on equal terms in the same sentence. In another place we have the tautology "syphilitic alopecia of the hair." These are not rare illustrations or they would not be worthy of mention. References to the literature are not nearly so abundant as would be expected in a comprehensive work of this sort, and they do not seem to have been collected with critical care. References to American dermatologic literature are surprisingly few. In one place a reference is made to "Richard and

Sutton." We knew that this eminent colleague was the equal of as many ordinary men as Homer's surgeon, but we had never seen him put in the plural before.

These criticisms, however, may be meticulous. The solid qualities of the book are beyond question, and they demand consideration for it by every one who would know the literature of dermatology.

DISEASES OF THE SKIN. By RICHARD L. SUTTON. Fourth Edition. Pp. 1132, with 969 illustrations in black and white and eleven illustrations in colors. St. Louis: The C. V. Mosby Company, 1921.

Sutton comes to us promptly with a new, fourth, edition of his book. The new edition differs only in such modifications as would be expected; the character and make-up of the book are unchanged. With succeeding editions his work is increasing rapidly in size: the last edition contained 1084 pages, this one contains 1132; the last contained 910 illustrations in black and white, this one contains 969. There is no change in the number of colored plates. What has been said of previous editions applies to this one. It is a good book, the work of an indefatigable student of dermatology. The make-up, from the publisher's standpoint, is unusually good. Both Dr. Sutton and his publishers are to be congratulated on the work.

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